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EPN (0-Ethyl-0-(P-Nitrophenyl) Phenylphosphonothioate) Decision Document

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U.S. Environmental Protection Agency

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This Special Review Document addresses the risks and benefits of pesticide products containing the subject active ingredient. The Agency has determined that the use of products containing the subject active ingredient may meet or exceed a risk criterion described in 40 CFR Part 154. Potential hazards will be examined further to determine the nature and extent of the risk, and considering the benefits of the subject active ingredient, whether such risks cause unreasonable adverse effects on the environment.

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EXECUTIVE SUMMARY

This Decision Document details the scientific basis which supports the Agency's proposed regulatory decisions relating to the future registration status of pesticides containing O-Ethyl-O-(p-nitrophenyl) phenylphosphonothioate (EPN). EPN is a broad spectrum insecticide currently used almost exclusively on cotton, field and sweet corn, and soybeans, although it is also registered as a mosquito larvicide, as well as for application on a variety of other food crops. All liquid and dry (granular and wettable powder) formulations of EPN greater than 4 percent are currently classified for restricted use. Taking into account considerations of actual use patterns--99 percent of EPN used in the U.S. is reportedly used on cotton, corn, and soybeans--the Agency proposes to continue registrations of EPN food uses subject to certain standardized label requirements and use practice prohibitions, as follows: 1) prohibit use of human flaggers unless in totally enclosed vehicles; 2) standardize label requirements for protective clothing, including goggles and a respirator, the phrase protective clothing required to appear prominently in bold face type on the label; 3) require, in the "Use Directions" section of the label, a specific warning against application of EPN when weather conditions favor drift; 4) require label

FIGURES

Page

Figure 1 Structural Formula for EPN II-1

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warnings specific to crop sites in order to minimize exposure to honeybees. Finally, the Agency intends to cancel use of EPN as a mosquito larvicide. The collective economic impact of the regulatory actions outlined above is projected as negligible.

These regulatory actions are based on the Agency's findings concerning the nature of the risks associated with EPN, the levels of exposure to the general public as well as to workers involved in applications procedures, and the economic benefits derived from EPN use. The Agency has determined that EPN poses the following risks to humans and the environment: 1) delayed neurotoxicity; 2) reductions in local/regional populations of nontarget organisms (honeybees); and 3) acute toxicity to aquatic organisms (mosquito larvicide use only). A quantitative assessment has been conducted of the delayed neurotoxic risk posed 1) to the general public as a result of EPN residues on food commodities derived from cotton, corn, and soybeans, and 2) to workers subject to dermal and respiratory exposure as a result of involvement in EPN application procedures. Because of uncertainty in determining a single NOEL, the Agency used a range of NOEL's to calculate a margin of safety range. Given current use patterns, the Agency has determined that an ample margin of safety exists for dietary exposure to the crops on which EPN is used. Likewise, ample margin of safety exist for the following applicator groups, and current use practices, provided that protective clothing is worn: pilots, mixer/loaders, and ground applicators. An ample margin of safety does not exist for human flagger, however, this problem can be corrected by requiring that flagging be by fully automated mechanical means or by humans working in totally enclosed vehicles. See chapter IV, Section C on Human Risk Assessment for a discussion of the margins of safety.

The Agency's analysis of the economic benefits associated with EPN have led to the following conclusions concerning major uses. Cancellation of EPN uses on cotton, soybeans, field corn, and sweet corn would in each instance result in increased treatment costs for growers currently using EPN, though in relative terms these impacts are classified as minor. Impacts passed on to processors and marketplace consumers are projected as negligible. The economic benefits associated with all other food uses of EPN are, for the most part, potential benefits. The only minor food uses for which any present usage and benefits can be addressed at all in quantitative terms are pecans (on which EPN is currently used by small numbers of growers in Alabama, Georgia, Oklahoma, South Carolina, Tennessee, and Texas) and peaches (on which small amounts of EPN are used in Georgia). In the case of pecans, minor economic benefits to growers can be attributed to EPN use in that some growers would absorb substantially increased treatment costs due to more costly alternatives, while others would experience decreased treatment costs, depending on the alternatives chosen. In the case of peaches, an EPN cancellation could be expected to decrease the treatment costs to producers. Consumer prices for pecans and peaches would not be affected.

Regarding EPN use as a mosquito larvicide, the Agency has concluded that economic benefits are negligible. As a mosquito larvicide, EPN has been used in recent years only in California, where an annual average of 68 pounds active ingredient were used during the period 1974-1979. EPN is not currently used in the mosquito abatement program in that State.

In connection with the dietary hazard, the risk/benefit analysis leading to the regulatory decision in this document is based on EPN applications to cotton, soybeans, and field and sweet corn, which as indicated above represent 99 percent of the EPN used in this country. (Small, localized use on pecans and peaches is considered insufficient to impinge on the average diet in the U.S.). Any risk/benefit analysis of potential uses is necessarily hypothetical at this juncture. The Agency remains concerned, however, about potential dietary exposure and risk in the event that EPN use patterns should significantly change. In addition to the uses discussed above, EPN is registered for the following food crops for which established tolerances (maximum permissible residue levels) are listed in 40 CFR 180.119: apples, apricots, beans, beets/beet greens, blackberries, boysenberries, cherries, citrus fruits, corn, dewberries, grapes lettuce, loganberries, nectarines, olives, pears, pineapples, plums (fresh prunes), quinces, raspberries, rutabagas, spinach, strawberries, sugarbeets, tomatoes, turnips/turnip greens, youngberries, almonds, and walnuts. Pursuant to the Pesticide Residue Amendment to the Federal Food, Drug, and Cosmetic Act (section 408), the administration of which is charged to the Environmental Protection Agency, the Agency has determined that EPN tolerances require reassessment. Data necessary to reassess EPN tolerances is required.

I. INTRODUCTION

A. General Background and Organization of this Decision Document

The Federal Insecticide, Fungicide, and Rodenticide Act as amended (FIFRA), 7 U.S.C. 136 et. seq., and regulations inplementing it require the Environmental Protection Agency (EPA) to review the risks and benefits of the uses of pesticides. On September 19, 1979, EPA issued a Notice of Rebuttable Presumption Against Registration and Continued Registration (RPAR) of pesticide products containing EPN, chemically known as O-Ethyl-O-(p-nitrophenyl) phenylphosphonothioate (EPA, 1979a). The rebuttable presumption was based on studies showing that EPN produced delayed neurotoxic effects in test animals, and is acutely toxic to aquatic organisms.

In addition to these risks, the RPAR notice listed five other possible adverse effects of EPN for which insufficient evidence existed at that time to initiate a rebuttable presumption. These included teratogenic effects, cholinergic effects, disorders of the eye, possible mutagenic effects, and reductions in populations of nontarget organisms (honeybees). The existence of a data gap for oncogenic effects was also noted. In addition, the RPAR Notice noted EPN's ability, when used in combination with another insecticide, to potentiate the effect, i.e., cause the total effects of the two chemicals to be greater than the sum of the two effects taken independently. The Position Document 1 (PD-1) issued with the Notice of Rebuttable Presumption describes these studies in detail.

The Agency invited rebuttal or other comments on the risks identified in PD-1 bearing on the presumption against EPN registration. The comments received and the Agency's response to them are contained in Appendix A.

The Agency also requested registrants and other interested parties to submit data on the other possible adverse effects of EPN. The comments received on these five additional possible adverse effects are also discussed in Appendix A.

This Decision Document addresses the risk and benefits of EPN, and proposes a final regulatory decision for the uses of EPN.[1]

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[1] EPN is registered for use as an insecticide-acaricide on a large number of agricultural crops; it is also registered for ground and aerial application as a mosquito larvicide by Mosquito Abatement Districts, Public Health Officials, and other trained personnel of Public Mosquito Control Programs. Although registered for use on numerous agricultural crops, EPN is used mainly on cotton; except for field and sweet corn and soybeans, its use on other food crops is negligible (EPA, 1979a; Memo, 1979).

This document contains six chapters. Chapter I is this introductory section. Chapter II discusses the chemical and environmental characteristics of EPN. Chapter III assesses the potential ecological effects risk from the use of EPN. Chapter IV assesses the potential human risks. Chapter V estimates and summarizes the economic benefits of EPN and describes the assumptions and limitations of these estimates. Chapter VI describes the possible regulatory options and modifications to reduce the risks of EPN and sets forth the final decision selected by the Agency.

B. Legal Background

1. The Statute

Under FIFRA Section 3(a) [7 U.S.C. 136a (a)], all pesticide products must be registered before they may be sold or distributed. Before the Administrator may register a pesticide product, however, he must determine that its use will not result in "unreasonable adverse effects on the environment," which is defined by section 2 (bb) of FIFRA to mean "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide." In other words, any decision about pesticide registration or continued registration must take into account both the risks and the benefits of the use of the pesticide.

Section 6 (b) of FIFRA authorizes the Administrator to issue a notice of intent to cancel the registration of a pesticide or to change its classification if it appears that the pesticide or its labeling "does not comply with the provisions of [FIFRA] or, when used in accordance with widespread and commonly recognized practice, generally causes unreasonable adverse effects on the environment." Thus, the Administrator may cancel the registration of a pesticide whenever he determines that it no longer satisfies the statutory standard for registration, which requires, among other things, that the pesticide not cause "unreasonable adverse effects on the environment" [FIFRA Section 3 (c)(5)(C)].

2. The RPAR Process

The Agency has designed a process, known as the Rebuttable Presumption Against Registration (RPAR) process, to gather risk and benefit information about pesticides which appear to pose unreasonable risk to human health or to the environment. This process, designed to allow an open, balanced decision with participation by all interested groups, is set forth in 40 CFR 162.11. These regulations describe various risk criteria, and provide that an RPAR shall arise if the Agency determines that any of the risk criteria have been met. Once a notice of rebuttable presumption has been published, registrants, applicants and other interested persons may submit evidence in rebuttal or in support of the presumption. Anyone may also submit evidence on the economic, social, and environmental benefits of any use of the pesticide. If the presumptions of risk are not rebutted, the benefits evidence submitted to or gathered by the Agency must be evaluated and considered with the risk information. The Agency also analyzes various risk reduction methods and their costs to determine if a pesticide's use may be regulated such that its risks are outweighed by its benefits. If an adequate balance between risks and benefits cannot be reached for a specific use, the registration for that use must be cancelled, or, in the case of a new application, denied.

II. CHEMICAL AND ENVIRONMENTAL CHARACTERISTICS

This chapter identifies the basic chemical and physical properties of EPN, including chemical composition and analytical method, persistence in soil and water, and potential for transport through the environment. More detailed evaluations of the potential exposure of humans and wildlife to EPN are presented in the Agency's Risk Assessment, found in chapters III and IV of this document.

A. Chemical Composition

EPN [O-Ethyl-O-(p-nitrophenyl) phenylphosphonothioate] is a non-halogenated, aromatic, phosphonothioate organophosphorous compound. The empirical formula for EPN is $C_{14}H_{14}NO_4PS$. The structural formula is shown in Figure 1 below. Other chemical names used by manufacturers are ethyl p-nitrophenyl thionobenzene phosphonate and O-Ethyl-O-p-nitrophenyl benzene thiophosphonate.

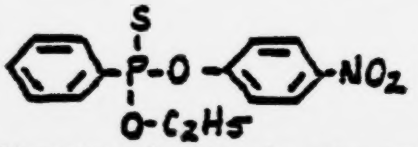

Figure 1. Structural Formula for EPN

The pure compound occurs as a light-yellow, crystalline powder with an aromatic odor, and the technical grade is a reddish-yellow, oily liquid. The chemical has a molecular weight of 323.3. EPN is only slightly soluble in water and is miscible with benezene, toluene, xylene, acetone, isopropyl alcohol, and methanol. The partition coefficient in octanol/water is 48.253. EPN has a melting point of 34.5°C, vapor pressure of 0.03 mmHg at 100°C, and specific gravity of 1.27 at 20°C. The hydrolytic half-life of EPN is 40.9 hours at a pH of 6 and temperature of 72°C ± 2°C (EPA, 1979a).

Colorimetric and gas chromatographic methods of analysis for quantitatively determining EPN residues in and on plant species have been devised by several researchers (EPA, 1979a). Bhagwat and Ramachandran (1974) described a simple and rapid spectrophotometric method for determination of EPN, EPNO, and p-nitrophenol in aqueous suspensions and enzymic digests. Other methods of analysis are cited in Kirkland and Pease (1967).

B. Environmental Characteristics

1. Persistence: Soils

Terriere and Ingalsbe (1953), using a mosquito larvae bioassay technique, analyzed for EPN deposits in the upper six inches of a sandy loam soil treated with 10 pounds of active ingredient per acre. Residues of 0.2 ppm EPN were found to persist in the soil after two years.

In a study of the persistence of ^{14}C EPN and ^{14}C parathion in the sand of a model ecosystem, EPN was found to be nearly three times as persistent as parathion. EPN comprised 84.5% of the total extracted ^{14}C from sand after 33 days. The remaining extracted ^{14}C products were amino-EPN$_2$ (0.4%), EPNO (0.574%), polar compounds (4.66%) and unknowns (9.88%) (EPA, 1979a).

A 1977 DuPont study reported that the half-life of intact ^{14}C EPN in soil ranged from two weeks in Dundee silt loam to one month in Keyport silt loam under actual field conditions in soil treated with 1.8 pounds active ingredient per acre. After four months, more than 90% of the residual radioactivity was in the upper 0- to 3-inch layer in both types of soil. The only metabolites found were those possessing the phenylphosphonic acid moiety. In greenhouse soil studies, the half-life of intact EPN on Fallsington sandy loam was reported to be five to six weeks (EPA, 1977a).

2. Persistence: Water

EPN hydrolyzes less slowly than other organophosphate compounds. It has a hydrolytic half-life of 40.9 hours at a pH of 6 and temperature of $72^{\circ}C \pm 2^{\circ}C$. Acute toxicity data available to the Agency show that the 96-hour LC_{50} for aquatic vertebrates range from 16.5 to 80 ppb. EPN appears to be more toxic than other organophosphates to aquatic invertebrates. (EPA, 1977a)

3. Bioaccumulation

EPN bioaccumulates in certain organisms. A model ecosystem study showed that EPN accumulates in organisms to a higher degree than parathion but accumulates less than leptophos and desbromoleptophos. EPN ecological magnification [2/] values were 73 for alga, 77 for daphnia, 12,561 for snails, 315 for mosquitoes, and 346 for fish (*Gambusia*) (EPA, 1977a).

Average bioconcentration factors of 260 in spot (*Leiostoma xanthurus*) and 756 in pinfish (*Logodon rhamboides*) were reported in 96-hour toxicity tests (EPA, 1977a).

An EPN uptake/depuration study reported a bioconcentration factor of approximately 700 X in pinfish. EPN was readily concentrated in the tissues of the fish to an equilibrium concentration of approximately 1.7 ug/g (1.7 ppm). Within one week after termination of the exposure, no EPN was detected in the tissues (EPA, 1977a).

4. Transport

Data available to the Agency show that there is little movement of EPN in soil. (EPA, 1977a).

[2/] "Ecological magnification" and "Bioconcentration" are here defined as the concentration of the parent compound in the organism as compared to concentration in water.

III. ECOLOGICAL EFFECTS RISK ASSESSMENT

In Position Document 1, the Agency based its rebuttable presumption against EPN on acute toxicity to aquatic organisms, but also listed another possible ecological effect for which insufficient information existed to begin a rebuttable presumption. That effect was reductions in populations of nontarget organisms (honeybees). The Agency has reviewed the rebuttal comments regarding the risk of reductions in populations of honeybees and has concluded that there is an acute risk from EPN use. However, the Agency has determined that this hazard can be mitigated by implementing certain amendments to the terms and conditions of registration short of cancellation.

EPN is registered for direct application to water as a mosquito larvicide by Mosquito Abatement Districts, Public Health Officials, and other trained personnel of Public Mosquito Control Programs (EPA, 1979a). Recommended application rates for EPN as a mosquito larvicide are 0.05 to 0.1 pounds active ingredient (a.i.)/acre, using ground or aerial equipment (EPA, 1979a). The Agency cited six (6) studies in the EPN Position Document 1 (EPA, 1979a) on the acute toxic effects of EPN to aquatic organisms. These studies showed that application of EPN at the highest recommended rate for larvicidal use (0.1 pounds a.i./acre) will result in an EPN concentration of 73.4 ppb in a 6-inch layer of water, which exceeds 1/2 the LC$_{50}$ 3/ or TLm 4/ for all seven (7) fresh water and estuarine aquatic organisms cited in the studies as representative aquatic species likely to be exposed to EPN mosquito larvicides. 5/ Application at the lowest recommended rate for larvicidal use (0.05 pounds a.i./acre) will result in an EPN concentration of 36.7 ppb in a 6-inch layer of water, which exceeds 1/2 the LC$_{50}$ of all species cited but the bluegill sunfish.

3/ LC$_{50}$ is the lethal concentration to 50% of the population. 40 CFR 162.11(a)(3)(i)(B)(3) provides that a rebuttable presumption shall arise if a pesticide's use "(r)esults in a maximum calculated concentration following direct application to a 6-inch layer of water more than 1/2 the acute LC-50 for aquatic organisms representative of organisms likely to be exposed as measured on test animals specified in the Registration Guidelines".

4/ TLm is the median tolerance limit.

5/ The seven representative aquatic species cited and their TLm or LC$_{50}$ were:

Species	1/2 Toxicity Value (ppb)	
Juvenile striped bass (*Morone saxatilis*)	(96 hr./TLm)	30
Spot (*Leistomus xanthurus*)	(96 hr./LC$_{50}$	12.8
Bluegill sunfish (*Lepomis maorochirus*)	(96 hr./LC$_{50}$	40
Pinfish (*Lagodon rhomboides*)	(96 hr./LC$_{50}$	8.2
Scud (*Gammarus lacustris*)	(96 hr./LC$_{50}$	7.5
Pink shrimp (*Penaeus duorarum*)	(96 hr./LC$_{50}$	0.15
Daphnia (*Daphnia magna*)	(48 hr./LC$_{50}$	0.16
(*Daphnia pulex*)	3 hr./TLm	0.6
(*Moina macrocopa*)	3 hr./TLm	3.55

The Agency has reviewed the two (2) currently registered mosquito larvicide labels. One label (Registration Number 2935-346) does not specify any use site. The other label (Registration Number 7001-7720) allows for application to standing water such as irrigated pastures or swamps. The Agency believes that these open-ended or non-existent use-site restrictions would enable (legally) EPN to be applied to aquatic habitat containing valuable fisheries resources. This review also revealed that these labels do not contain explicit hazard warning statements. One label (Registration Number 7001-7720) was found to contain no statement of toxicity to aquatic species and no statement prohibiting application to any body of water.

Based on its review of the current EPN mosquito larvicide labels, the Agency concludes that the existing use restrictions and precautionary statements do not assure that the risk criterion for aquatic organisms will not be exceeded.

IV. HUMAN EFFECTS RISK ASSESSMENT

In Position Document 1, the Agency based its rebuttable presumption against EPN on delayed neurotoxic effects, but listed four other possible adverse effects to humans for which insufficient information existed to begin a rebuttable presumption. Those other effects were: 1) teratogenic effects; 2) cholinergic effects; 3) disorders of the eye; and 4) possible mutagenic effects. The existence of a data gap for oncogenic effects was also noted. The Agency has reviewed the rebuttal comments regarding these other adverse effects and has concluded that:

1) The available information shows an obvious data gap for teratogenic effects which should be filled by performing teratogenic studies in rats and rabbits during the normal reregistration procedure.

2) EPN does not produce primary cholinergic activity (EPA, 1980e). EPN produces clinical signs of toxicity secondary to its inhibition of cholinesterase. These signs are a result of accumulation of acetylcholine in the organism and are cholinergic responses. But there is no evidence that EPN produces direct cholinergic effects by acting on the cholinergic receptors of the organism.

3) There is no evidence to indicate that EPN can cause disorders of the eye (EPA, 1981c).

4) There is no evidence to show that EPN or p-nitrophenol are mutagenic agents (EPA, 1980e).

5) Studies on the oncogenic potential of EPN are not available and an oncogenic data gap exists (EPA, 1980e).

EPN has been shown to produce organophosphorus-type delayed neurotoxicity in chickens[6] under experimental conditions. Organophosphorus-type delayed neurotoxicity is very serious in that it produces irreversible nerve damage that is crippling. It is characterized by the following properties: a delay in the order of 10-14 days between a single effective dose and the appearance of clinical and histopathological signs; the appearance of the delayed effect well after recovery from the acute toxicity of the compound; no apparent relationship between the compound's ability to inhibit blood cholinesterase and its ability to produce the delayed effect; the appearance of abnormalities in gait which may proceed to complete paralysis and are generally irreversible; and the destruction of nerve axons in the spinal cord and the subsequent disappearance of the myelin sheath which surrounded the lost axons. The delayed toxic effect can also be produced by daily administration of doses which individually will not produce the toxic response, i.e., the toxicity is cumulative. It would be prudent, therefore, to consider the possibility of a delayed neurotoxic risk to humans. This chapter presents the Agency's assessment of potential risk to human health posed by the continued use of EPN. A brief discussion of the laboratory studies is provided in Part A; the Agency's analysis of potential human exposure is presented in Part B; the Agency's human exposure risk analysis is presented in Part C. Estimates of risk, such as those presented in this chapter, can only be taken as an indication of the possible relative magnitudes of risk but should not be considered as absolute levels of risk.

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[6] Early studies on the toxicity of tri-o-cresyl phosphate (TOCP), a compound that has demonstrated the delayed neurotoxic effect in humans, identified the chicken as a species susceptible to the delayed neurotoxic effect. Subsequently, the chicken was found to be sensitive to mipafox and leptophos; compounds that have also demonstrated the delayed neurotoxic effect in humans. Studies with the chicken found these results to be reproducible from laboratory to laboratory and to be related to dose, dose regimen, and route of adminstration.

Many mammalian species have been tested for this effect with negative results in rats and mice, and positive but inconsistent or atypical results with dogs and cats. Other species, such as bovines and primates, have shown positive results, but it is neither practical nor economically feasible to use them for determining a no-observed effect level (NOEL).

At present, there is no clear-cut information as to why the chicken is a sensitive species, nor is it possible to correlate the chicken's response with the human response beyond the three compounds (TOCP, mipafox, and leptophos) known to be active in humans. At this time the chicken, despite its recognized deficiencies, is the best model for organophosphate-type delayed neurotoxicity available.

A. Delayed Neurotoxicity of EPN

The Agency's overall conclusion concerning the delayed neurotoxicity of EPN is based on the results of several studies which demonstrate that exposure to EPN results in delayed neurotoxicity in chickens and one study which demonstrates that exposure to chronic low doses of EPN results in depression of plasma and RBC cholinesterase activity in humans.

In the EPN Rebuttable Presumption Against Registration (RPAR) issued in September, 1979, the Agency cited 12 studies[7] on the delayed neurotoxic effects of EPN in chicken and two studies on such effects in rodents. Six of the studies in chickens were of acute effects after a single dose; two of the studies in chickens were of acute effects after two doses 21 days apart; and the remaining six were subchronic or chronic studies of effects after repeated treatment ranging from 28 days to 85 weeks. The two rodent studies were of acute effects after a single dose.

The Agency has evaluated the rebuttal comments submitted in response to the RPAR (See Appendix A) and information which has become available since the issuance of the RPAR[8] and has concluded that the risks from EPN use can be mitigated by implementing certain amendments to the terms and conditions of registration short of cancellation.

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[7] Experiments done by the Communicable Disease Center (CDC) counted as a single study.

[8] Subsequent to the publication of the EPN RPAR, the three basic producers of EPN (DuPont, Marubeni, and Velsicol) sponsored a repeat of the Abou-Donia and Graham (1978) study at Huntingdon Research Center. This subchronic delayed neurotoxicity study was received by the Agency on March 24, 1982. The study is summarized in Section A. 2. of this chapter.

1. Studies Cited in the September, 1979, EPN RPAR

The studies on the delayed neurotoxic effects of EPN cited by the Agency in the September, 1979, EPN RPAR document (Position Document 1) are summarized in tables IV-1 and IV-2 below.

Subsequently a new study on EPN delayed neurotoxicity has been submitted. This study is described in detail below.

2. Huntingdon Research Center (1982)

This study was designed to provide additional information as to the neurotoxicity of EPN using TOCP as a positive control. The study consisted of two parts-- a range finding study and the main study. A total of 271 adult domestic hens (Gallus domesticus) were used -- 50 in the range finding study, 10 for a detailed health check, and 211 in the main study (including 13 replacement birds). The birds were housed in treatment groups in floor pens measuring 1.5 m x 2.3 m. All doses of EPN and TOCP were administered orally by gelatine capsule. Individual bird doses were calculated on the basis of body weight and were adjusted on a weekly basis to allow for changes in body weight. Acetone (distol) was used as the vehicle for EPN and corn oil as the vehicle for TOCP.

Table IV-1. Studies on Delayed Neurotoxic Effects of EPN in Chickens Cited in Position Document 1

Study	Material	Dose	LD-50	# birds per test group	Method of Administration	Period of Administration	Results		
							Ataxia	Paralysis	Histopathology
CIC (Undated) (Report #8)	EPN	5, 10, 20, 40, 60, 80, 160, 320, 640, and 1280 mg/kg	>60 mg/kg (estimate)	10 at 60 mg per kg; 2 at other doses	intraperitoneally	single dose	at doses 40 thru 1280 mg per kg (muscle weakness)	no	not performed
Durham et. al. (1956)	EPN	Ranged 5 to 1280 mg/kg	860 mg/kg	28 total	subcutaneously	single dose	yes (21 birds); all birds (10) at 60 mg/kg ; 40 mg/kg minimum dose for this effect	no	not performed
Witter and Gaines (1963)	EPN tech.	60 mg/kg	not given	13 [?]	subcutaneously	single dose	depression of brain true and (or) pseudo-cholinesterase no ataxia	from 1st day to end of experiment (4 of 13 birds died between 11th & 29th day	not performed
Aldridge and Barnes (1966)	EPN)	10 mg/kg	not given	not given	subcutaneously	single dose	persistent weakness & ataxia, 10-16 days after dosing	no	characteristic lesions in spinal cord and sciatic nerves
Gaines (1969)	EPN tech.	20, 40, & 80 mg/kg	not given	not given	subcutaneously	single dose	lowest effective dose = 40 mg/kg; highest ineffective dose = 20 mg/kg	no	not performed
Ohkawa et al. (1977)	(±)-EPN (+)-EPN (-)-EPN	31.2, 40.6, 52.8, 68.6, & 89.2 mg/kg	(±) 17, (+) 12, & (-) 47 mg per kg	3 each dose level for each isomer	intraperitoneally	single dose	dosed with 20 mg/kg atropine sulfate to minimize acute effects	(+)-EPN, none; (-)-EPN, all at 68.6 & 89.2 mg/kg; 1 at 52.8 & 2 at 40.6 mg/kg; (±)-EPN, 2 at 89.2, & 1 each at 52.8 & 68.6 mg/kg	(-)-EPN dosed hens showed degenerating myelin sheaths & swollen, fragmented axons in sciatic nerve and spinal cord

Table IV-1. Studies on Delayed Neurotoxic Effects of EPN in Chickens Cited in Position Document 1 (Continued)

Study	Material	Dose	LD-50	# birds per test group	Method of Administration	Period of Administration	Results		
							Ataxia	Paralysis	Histopathology
IIT (1976)	EPN tech. 92.4%	28.8 mg/kg	28.8 ± 6 mg EPN/kg	10 per group (10 added to EPN group due to high mortality	gavage	two doses, 21 days apart	severe lethargy, anorexia, and severe ataxia after each dose	no behavioral signs of neurotoxicity	no treatment-related lesions
Kaneko and Sakamoto (1976)	EPN tech. 92.4%	0, 22.2, 20.0, 37.4, 28.8, 37.4, & 48.7 mg/kg	35.1 mg/kg	5 birds per group	intraperitoneally	two doses, 21 days apart	no	no	not performed
DuPont (1977) and DuPont (1979a)	EPN	0, 1, 5, 15 & 45 ppm EPN and TOCP	not given	50 birds per group	in diet	105 weeks	yes, at 45 ppm	no	EPN-related changes in spinal cord & brains
Frawley (1976)	EPN	50, 100, 200 & 400 ppm EPN; 5/100, 50/50, 25/25 & 10/10 TOCP/EPN; & 40/100 & 20/500 EPN/-malathion	not given	4 birds per group	in diet	7 months	yes, at 50 ppm EPN	yes, at 50 ppm EPN; no evidence of potentiation at 25/25 TOCP & EPN or at 20/500 EPN & malathion	spinal cords normal; treatment-related changes in sciatic nerve
Abou-Donia & Graham (1978)	EPN tech. 85%	0.01, 0.1, 0.5, 1.0, 2.5, 5.0, & 10 mg EPN/kg	10 mg/kg	6 birds per group	orally in gelatin capsules	daily for 90 days	all hens at 0.1 to 10 mg/kg; 5-21 days after administration; 0.01 mg/kg = NOEL	yes; 4 birds at 10 mg/kg at 7-66 days. One other bird at 10 mg/kg progressed to "near paralysis"	treatment-related change in peripheral nerve and spinal cord
Sakamoto (1977)	EPN tech. 92.4%	0, 1, 3, & 10 mg EPN/kg	28.8 ± 6 mg/kg	10 birds per group	orally ("forcibly")	daily for 28 days ("except Sundays")	yes, at 10 mg/kg; 3 mg/kg = NOEL	yes, at 10 mg/kg	not available at time of report

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Table IV-1. Studies on Delayed Neurotoxic Effects of EPN in Chickens Cited in Position Document 1 (Continued)

Study	Material	Dose	LD-50	# birds per test group	Method of Administration	Period of Administration	Results		
							Ataxia	Paralysis	Histopathology
CIC (Undated) (Report #9)	EPN tech.	20, 50, 100, 200, & 400 ppm EPN; control	not given	2 birds per group	in diet	120 days	yes; 1 each at 50, 100, & 200 ppm; both 400 ppm birds died of starvation	not specified	not performed
CIC (Undated) (Report #13)	EPN	0, 75, 150, & 300 ppm	not given	7 birds per group	in diet	400 days	yes; for some birds at all levels	yes; all birds at 300 ppm died within 6 days	not performed

Table IV-2. Studies on Delayed Neurotoxic Effects of EPN in Rodents Cited in Position Document 1

Study	Material	Dose	LD-50	# animals/ test group	Method of Administration	Period of Administration	Results
El-Sebae et al. (1977)	EPN 30%	20 mg/kg	not given	not given (mice)	orally	single dose	irreversible ataxia after 29 days
Francis 1977	EPN	10 mg/kg	40 mg/kg	3 (rats)	orally	single dose	acute symptoms hours after treatment; 2 rats markedly ataxic by day 2; complete recovery by day 6. No recurrence after one month.

Range Finding Study

The range finding study consisted of a 28-day dosing period and was designed to check the dose levels to be used in the main study. The dosing period was preceded by a 14-day settling-in period. Ten groups of five birds each were allocated to treatment. Group 1 was the vehicle control group. Groups 2,3, and 4 were the positive control groups and received TOCP at dose levels of 1.0, 5.0, and 10.0 mg/kg/day respectively. Groups 5,6,7,8,9, and 10 were the EPN treatment groups and received EPN at dose levels of 0.01, 0.1, 0.5, 1.0, 2.5, and 5.0 mg/kg/day respectively.

General bird health remained good throughout the experimental period.

The results of the range finding study are summarized in Table IV-3.

Main Study

The main study consisted of a dosing period of a minimum of 90 days followed by a 90-day recovery period. The first 10 birds in each of the 10 treatment groups were scheduled for sacrifice at the end of the dosing period and the remainder at the end of the recovery period.

Table IV-3 Results of Huntingdon Research Center's Range Finding Study on Delayed Neurotoxic Effects of EPN

Group[a] Number	Treatment	Dose Level (mg/kg/day)	Signs of Ataxia shown
1	Vehicle Control	0	No
2	TOCP	1.0	No
3	TOCP	5.0	Yes[b]
4	TOCP	10.0	Yes[c]
5	EPN	0.01	No
6	EPN	0.1	No
7	EPN	0.5	No
8	EPN	1.0	NO
9	EPN	2.5	Yes[d]
10	EPN	5.0	Yes[e]

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[a] Each group consist of 5 adult domestic hens (Gallus domesticus).

[b] One bird developed severe ataxia and was sacrificed at the beginning of day 20 as it was unable to stand. No other birds in this group showed any signs of ataxia.

[c] All birds in this group had developed ataxia by the end of the dosing period. Ataxia was moderate to severe in three of the birds and less severe in the remaining two birds.

[d] Four birds in this group showed some signs of ataxia. One bird was sacrificed at the end of Day 15 of the dosing period because it had become very weak.

[e] One bird in this group showed moderately severe ataxia by the end of the dosing period. No signs of ataxia were observed in any of the other three surviving birds. One bird died within three hours of being dosed. The cause of death could not be established.

Prior to the start of the main study, ten birds were taken at random from the available pool of birds-as a bird health check group. The reason for establishing this group was to ensure that the incidence of spontaneous lesions was within normal limits for the age of the birds used in the study. This group was designated "Group 1" in the main study, although the birds were not dosed at any time.

Birds for the main study were allocated to treatment groups 5 weeks before dosing commenced, but the report of the study only presented data for the 14-day period prior to the start of dosing. The extended settling-in period was a result of delays in starting the dosing phase of the study. Twenty birds were allocated to each of the ten treatment groups. Group 2 was the vehicle control group. Groups 3,4, and 5 were the positive control groups and received TOCP at dose levels of 1.0, 5.0, and 10.0 mg/kg/day respectively. Groups 6,7,8,9,10, and 11, were the EPN treatment groups and received EPN at dose levels of 0.01, 0.1, 0.5, 1.0, 2.5, and 5.0 mg/kg/day respectively.

Four birds died during the 14-day settling-in period and nine showed marked body weight loss during the same period. These 13 birds were replaced with birds from the available pool before the dosing commenced.

On the first day of dosing, birds in Groups 10 and 11 (EPN at 2.5 and 5.0 mg/kg/day respectively) appeared slightly unsteady within a few hours of being dosed. On the second day of dosing, birds in these same groups appeared rather subdued, but no clinical signs of toxicity were observed at the end of Day 2.

General bird health was good during the dosing period.

The results of the main study are summarized in Table IV-4.

For birds examined at the end of, or during the treatment period, treatment-related neuropathological changes were found in a dose-related fashion in groups 4 (TOCP at 5.0 mg/kg/day), 5 (TOCP at 10.0 mg/kg/day), 9 (EPN at 1.0 mg/kg/day), 10 (EPN at 2.5 mg/kg/day), and 11(EPN at 5.0 mg/kg/day). The induced changes were qualitatively similar with both test compounds. The lesions in the 1.0 mg/kg/day EPN dosage group were mild and only marginally greater than the level of spontaneous change found in control birds. The most severe changes were in the 10.0 mg/kg/day TOCP dosage group. However, comparison of results from the 5.0 mg/kg/day TOCP and the 5.0 mg/kg/day EPN dosage groups showed that EPN was marginally more neurotoxic at this dosage level.

Table IV-4 Results of Huntingdon Research Center's Study on Delayed Neurotoxic Effects of EPN.

Group[a] Number	Treatment	Dose Level (mg/kg/day)	Results Positive Signs of Ataxia Shown	 Treatment-related/ Dose-related Neuropathological Changes
1[b]	—	—	—	—
2	vehicle Control	0	No	No
3	TOCP	1.0[c]	No	No
4	TOCP	5.0	Yes[e]	Yes
5	TOCP	10.0	Yes[f]	Yes
6	EPN	0.01	No	No
7	EPN	0.1	No	No
8	EPN	0.5[d]	No	No
9	EPN	1.0	No	Yes
10	EPN	2.5	Yes[g]	Yes
11	EPN	5.0	Yes[h]	Yes

a/ Each group, except Group 1, consisted of 20 adult domestic hens (Gallus domesticus).

b/ Group 1 was the bird health check group. This group consisted of only 10 adult domestic hens (Gallus domesticus).

c/ 1.0 was considered the "no-effect" dosage for delayed neurotoxicity of TOCP, taking into account both pathological and clinical factors.

d/ 0.5 was considered the "no-effect" dosage for delayed neurotoxicity of EPN, taking into account both pathological and clinical factors. A review of the report by Agency scientists considered 0.01 mg/kg/day a NOEL based on consideration of subtle histological changes observed in the spinal cord. Thus, identifying a NOEL for this effect is a major point of contention in assessing the risk to humans.

e/ Four birds developed signs of ataxia.

f/ All birds in this group developed ataxia.

g/ One bird showed signs of ataxia on Day 26, 27, and 28. On Day 29 the bird was found dead.

h/ Eleven birds in this group showed positive signs of ataxia.

The conclusion drawn in the report of the study, taking into account both pathological and clinical factors, was that the "no-effect" dose for delayed neurotoxicity of EPN was 0.5 mg/kg/day and of TOCP was 1.0 mg/kg/day.

The EPA scientific reviewer of this study disagreed with this "no-effect" dose for EPN. The reviewer considered subtle histological changes observed in the spinal cord indicative of EPN effect at doses of 0.1 and 0.5 mg/kg/day. The reviewer concluded that 0.01 mg/kg/day was a "no-effect" dose for EPN in this study (Memo 1983a).

3. Summary

In summary, the registrant sponsored Huntingdon Research Center study and the studies cited by the Agency in PD 1 all demonstrate that EPN does produce delayed neurotoxic effects in chickens, and therefore may have the potential to produce the same effects in humans.

B. Human Exposure to EPN

This section on potential human exposure to EPN is divided into two subjects: 1) exposure to the general public; and 2) exposure to agricultural workers and other applicators. Where possible, the discussions are use-specific and the sources of exposure discussed are primarily associated with the major uses.

1. Exposure to the General Population

The most likely source of exposure to members of the general public from the use of EPN is primarily through consumption of treated crops. This section presents an assessment of potential dietary sources of exposure to EPN.

Dietary Exposure Analysis

The Agency has developed three scenarios of dietary exposure to EPN: 1) "worst case" -- maximum dietary burden in the event that EPN were used on all acreage of all crops for which it is registered, 2) "realistic worst case" -- maximum dietary burden as a result of EPN application on cotton, soybeans, and corn, the primary crops for which it is reportedly used, and 3) a "probable case" estimate of dietary exposure, based on residue data for these three major uses.

The maximum dietary burden in the event that EPN were used on all crops for which it is registered would be 0.017 mg/kg body weight (bw) per day for on average 60 kg individual. The calculations for each crop are given in Table IV-5, which equals 0.0164 mg/kg per day (rounded off to 0.016 mg/kg).

Table IV-5. Maximum Expected (Worst Case) Daily Dietary Exposure and Maximum Dietary Burden in the U.S.

Crop	Tolerance (ppm)	Food Factor	Theoretical Maximum Exposure to EPN (mg/day)	Theoretical Maximum Dietary Burden* to EPN for a 60-kg person in mg/kg bw/day
Apples	3.0	2.53	0.11385	189.7
Apricots	3.0	0.11	0.00506	8.4
Beans	3.0	2.04	0.09180	153.0
Beets	3.0	0.17	0.00782	13.0
Beet greens	3.0	0.03	0.00135	2.3
Blackberries	3.0	0.03	0.00135	2.3
Boysenberries	3.0	0.03	0.00135	2.3
Cherries	3.0	0.10	0.00460	7.7
Citrus Fruits	3.0	3.81	0.17154	285.9
Corn (all)	3.0	2.51	0.11295	188.3
Dewberries	3.0	0.03	0.00135	2.3
Grapes (incl. raisins)	3.0	0.49	0.02207	36.8
Lettuce	3.0	1.31	0.05887	98.1
Loganberries	3.0	0.03	0.00135	2.3
Nectarines	3.0	0.03	0.00135	2.3
Olives	3.0	0.06	0.00276	4.6
Peaches	3.0	0.90	0.04047	67.5
Pears	3.0	0.26	0.01150	19.2
Pineapples	3.0	0.30	0.01334	22.2
Plums (incl. prunes)	3.0	0.13	0.00598	10.0
Quinces	3.0	0.03	0.00135	2.3
Raspberries	3.0	0.03	0.00135	2.3
Rutabagas	3.0	0.03	0.00135	2.3
Spinach	3.0	0.05	0.00230	3.8
Strawberries	3.0	0.18	0.00828	13.8
Sugar (cane & beet)	3.0	3.64	0.16372	272.8
Tomatoes	3.0	2.87	0.12937	215.6
Turnips	3.0	0.05	0.00230	3.8
Turnip greens	3.0	0.03	0.00135	2.3
Youngberries	3.0	0.03	0.00135	2.3
Almonds	0.5	0.03	0.00023	0.4
Cottonseed	0.5	0.15	0.00112	1.9
Pecans	0.5	0.03	0.00023	0.4
Walnuts	0.5	0.03	0.00023	0.4
Soybeans	0.05	0.92	0.00069	1.2
		Totals	0.99 mg/day	0.016 mg/kg/day

* Column multiplied by 10^{-5} to eliminate zeros; for correct figure, multiply individual dietary burden figures by 10^{-5}.

The maximum dietary burden, as calculated in Table IV-5, assumes that EPN residues could exist on each commodity at the tolerance level[9] (EPA, 1981e). The maximum dietary burden is not likely ever to be exceeded in standard agricultural practice following label instructions. In Table IV-5, the maximum rate of exposure is calculated as 0.99 mg/day per person.

Based on tolerances for cotton, corn, and soybeans, the sum of the dietary burdens for these crops was calculated to be 1.65×10^{-3} mg/kg per day. Below, each of these crops is calculated separately with the percent of the U.S. crop actually treated with EPN formulations factored in. These results are presented in Table IV-6 as a "Realistic Worst Case." The rate of ingestion of EPN, under these conditions of tolerance levels and percent crop treated factored in, is 2.2×10^{-2} mg/day which corresponds to a dietary burden of 3.6×10^{-4}mg/kg per day in the "Realistic Worst Case"

9/ A tolerance is the maximum permissible residue level allowable after treatment with a pesticide. Tolerances for pesticides are set by EPA and enforced by the Food and Drug Administration (FDA) and the United States Department of Agriculture (USDA . Current permanent tolerances for EPN are listed in 40 CFR 180.119.

Table IV-6. Realistic Worst Case Dietary Exposure

Crop	Assumed Residues (ppm)	% Crop Treated	Food Factor (%)	Exposure Rate (mg/day)	Dietary Burden (mg/kg/day
Cotton	0.5	65.8	0.15	0.00074	0.000012
Sweet Corn	3.0	20.7	2.25	0.02095	0.00035
Soybeans	0.05	1.1	0.92	0.0000076	0.00000013
			TOTALS	0.022	0.00036

Table IV-6. Realistic Worst Case Dietary Exposure

Crop	Assumed Residues (ppm)	% Crop Treated	Food Factor (%)	Exposure Rate (mg/day)	Dietary Burden (mg/kg/day
Cotton	0.5	65.8	0.15	0.00074	0.000012
Sweet Corn	3.0	20.7	2.25	0.02095	0.00035
Soybeans	0.05	1.1	0.92	0.0000076	0.00000013
			TOTALS	0.022	0.00036

Based on residue data submitted by Dupont, "probable case" exposure to EPN was recalculated. These estimates were made on the basis of residues in corn (sweet, pop, and oil), cottonseed (oil, margarine, and shortening), and soybeans (oil, margarine and shortening). These results and the assumptions used in the calculations are presented in Table IV-7. The calculation of the dietary uptake from corn, cottonseed, and soybeans is 3.11×10^{-3} mg/day and the dietary burden for a 60-kg average individual is 5.2×10^{-5} mg/kg per day.

If a similar calculation is made for a 70-kg individual, the dietary burden is 4.4×10^{-5} mg/kg per day (assuming the same calorie intake).

Table IV-8 summarizes the possible dietary exposure scenarios for EPN, under three different conditions: 1) Worst Case, 2) Realistic Worst Case, and 3) Probable Case.

"Probable case" dietary calculations, based on residue data on food commodities derived from cotton, soybeans, and corn treated with EPN, represents the Agency's best estimate of dietary exposure at this juncture, in view of available information on current use patterns. This determination represents the Agency's best judgement, taking into account uncertainties about undetermined, finite residues of EPN

Table IV-7. Probable Case Dietary Intake of EPN

Crops	Expected Residues (ppm EPN)	Crop or Commodity	Food Factor (%)	Dietary Intake (mg/day) d/
Corn	≤ 0.02[a]	Sweet, pop, oil, and meal oil	2.52	≤ 0.00076
Cotton-seed	≤ 0.43[b]	Oil, margarine, and shortening	0.15	0.00097
soybeans	≤ 0.10[c]	Oil, margarine, and shortening	0.92	≤ 0.00138
		Total:		0.00311 mg/day

a/ Limit of detection =0.02 ppm.

b/ This estimated level of EPN assumes the following: 1) no oil processing of crude to refined oil; 2) no losses in fractionation into cottonseed oil and meal and processing of oil; 3) average raw agricultural commodity (rac) EPN residue is 0.069 ppm on cottonseed 7 days (post harvest interval) following the last application; 4) a concentration factor for EPN residues from cottonseed to cottonseed oil is 6.25 x. The EPN concentration in cottonseed oil would then be estimated to be 0.3 ppm (0.069 x 6.25).

c/ Expected average soybean oil concentration from data presented assuming no processing of crude soybean oil to refined oil.

d/ Daily Dietary Intake (mg/day) = residue found x food factor x 1.5 kg/day x 10^6 mg/kg occuring in meat, milk, and eggs, and questions raised by FDA surveillance data about EPN use on crops on which no usage has been reported. (See Table IV-9)

Reported usage of EPN on crops other than cotton, soybeans, and corn is very low and could not be expected to impinge on the average U.S. diet. Reportedly there are 66,000 treatment-acres of pecans treated with EPN in the U.S. Since EPN is not applied until the nut hardens, no residues of EPN are expected in the kernel. Additionally, the percent of crop treated for pecans is low, approximately one percent.

Very small and localized treatments are made on peaches (1,600 acres), beans (2,300 acres), and tomatoes (200 acres). While known use of EPN on other than major use crops would not be expected to significantly affect dietary exposure, questions about actual use patterns have been raised by FDA monitoring studies which reported findings of EPN residues in peanuts, baby food, apples, onions, muffin

Table IV-8 Summary Chart of EPN Dietary Exposure

Exposure Scenario	Dietary Burden for Average 60-kg U.S. Individual (Mg/Kg/day)	Comments
Worst Case (Table IV-5	1643×10^{-5}	Upper limit of daily dietary burden (DB). Assumes all crops have EPN at tolerance levels and that each crop is 100% treated with EPN formulations.
Realistic Worst Case (Table IV-6	36×10^{-5}	Assumes corn, cotton, and soybeans are the main crops of concern and takes into account the % of these crops actually treated with EPN. Residues assumed at tolerance levels.
Probable Case (Table IV-7)	5.2×10^{-5} (4.4×10^{-5} for a 70-kg individual)	Residue levels (corn, cotton, and soybeans) determined from rebuttal studies. This constitutes the Agency's best estimate of DB on present data

mix, and trout (memo, 1980a). The EPN residues detected by the FDA Surveillance Program are very low (trace or parts per billion). See Table IV-9. However, it should be emphasized that only a small portion of each crop is sampled and analyzed by the FDA, and positive determinations are generally recognized as indications of residue problems.

The Agency views entrance of EPN and EPN metabolites into animal feeds as likely and believes that finite residues of EPN could occur in meat, milk, and eggs, but the exact levels of EPN cannot be established with certainty at this time in these commodities. However, it is expected that residues of EPN will most likely not occur at significant levels. Hence, contributions from these commodites were not factored into the probable case dietary calculations.

In view of the considerations summarized above, the Agency has based its present assessment of dietary risk (Section IV. C.1 below) on "probable case" exposure to EPN. The "probable case" assumes that corn, cotton, and soybeans are the main crops of concern since reported usage of EPN on crops other than these three is very low and could not be expected to impinge on the average U.S. diet. In the

Table IV-9. FDA Sampling Results: Surveillance Program

FY period	No. of Positive Samples	Concentration of EPN (ppb)
'79	1 (apples)	60
'78	0	--
'77	1 (trout)	60
	1 (muffin mix)	170
	1 (onions)	40
'76	0	--
'75	1 (apples)	trace
	1 (baby food)	trace
	1 (peanuts)	180
	1 (peanuts)	200
'74	0	--
'73	0	--
'74	0	--

"probable case" scenario the Agency takes into account the percent of corn, cotton, and soybeans actually treated with EPN and assumes that residues are at tolerance levels. The Agency calculated the dietary burden for a 70-kg individual to be 4.4 x 10^{-5} mg/kg/day in this scenario. However, the Agency again reaffirms its concern about potential dietary exposure should EPN be used on all crops for which it is registered.

2. Occupational Exposure to EPN

This section of the Decision Document evaluates potential occupational exposure resulting from the use of EPN. The Agency has identified human populations occupationally exposed to EPN and has identified the type and probable extent of their exposure. In this analysis, only two avenues of exposure are considered: respiratory and dermal. However, individuals occupationally exposed to EPN are also subject to the same types and amounts of nonoccupational exposure as members of the general population.

The group at risk from inhalation and dermal exposure to EPN include those involved in aerial and ground application (airplane pilots, mixers/loaders, and flaggers). Potential exposure also exists for field workers, insect scouts, and unprotected by-standers.

The Agency has revised its exposure analysis in light of the rebuttals received in response to the PD 1 (EPA, 1981b; EPA, 1981d). The basic change is that the Agency's revised exposure estimates now assume that application personnel wear protective clothing and a respirator as called for by the label.[10]

The Agency's inhalation and dermal exposure estimates in Position Document 1 were based on data from the Velsicol (1979b) exposure study which failed to take into account the use of protective clothing by personnel involved in EPN application [See Table IV-10]. In effect, the Agency based its assessment on a theoretically "worst case" situation unrelated to standard application practices.

In Velsicol's exposure study, pilots, loaders, flaggers, and ground applicators were monitored for respiratory and dermal exposure during both aerial and ground applications of EPN to cotton. Dermal exposure was estimated by affixing denim patches to the applicator's clothing and monitoring

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[10] The label directions for most EPN formulations have been revised to include protective clothing and respirators. Most current labels specify approved respirators, while some specify either a mask or a respirator. In addition, most formulations of EPN have been classified for restricted use.

Table IV-10. Applicator and Support Personnel Exposure to EPN During Application to Cotton

Workers	Dermal Exposure (mg/kg per hr.)		Inhalation Exposure (mg/kg per hr)	
	High	Low	High	Low
Pilots (4)a/	0.009	0.0016	0.000023	0.000015
Loaders (3)a/	0.026	0.0015	0.000032	0.000019
Flaggers (3)a/	0.46	0.053	0.021	0.000025
Ground Applicators (2)a/	0.028	0.0038	0.00012	0.000021

a/ Number of workers monitored. High and low exposure values are based on the highest and lowest exposure for the workers monitored.

the quantity of EPN which adhered to the patches. Dermal exposure to various parts of the body was then predicted, based on normalizing the residue data from nearby patches to the known surface areas of any given body part. The one exception to this procedure involved dermal exposure to the hands, in which EPN residue data were compiled and presented in two separate ways.

1) A "worst case" estimate of dermal exposure which was based on the sum for the total predicted residues for the face, back of neck, front of neck, "V" of chest, forearms, and hands.

2) A "potential exposure" estimate was developed by summing all predicted dermal residues from all skin surfaces.

The "potential exposure" estimates given in Position Document 1 were obviously unrealistic since in effect they estimated exposure of a naked applicator, and hence were useful for comparative purposes only. Based on the rebuttal comments, the Agency has revised the original estimates based on the assumption that protective clothing and a respirator are worn routinely and that miscompliance occurs infrequently.

By assuming the face, front of neck, back of neck, and "V" of chest are exposed, the following summary of the Velsicol Exposure Study (Velsicol, 1979b) can be made. Table IV-11 summarizes daily exposure to EPN based on the Velsicol Exposure Study.

In Table IV-12 below, these data are combined to give a high and low range of exposure for each personnel category, while Table IV-13 shows (by crop) the estimated number of workers in each applicator group exposed to EPN.

Table IV-14 combines the data from Tables IV-12 and IV-13 into a comprehensive summary table (similar to Table 10 in Position Document 1) including data on the numbers of applicators and the days per year that they are likely to work.

C. Human Risk Assessment

In the following section, the Agency discusses problems in developing a theoretical delayed neurotoxic risk for EPN, and then presents estimates of such risk resulting from the use of EPN: 1) to the general population from exposure to EPN residues in contaminated food; and 2) to workers exposed during application of EPN.

Table IV-11. Dermal Exposure to EPN (ug)

Personnel	Face	Back of Neck	Front of Neck and "V" of Chest"	Total
Mississippi Study				
Pilot -1	63	11	15	89
Pilot -2	32	5	7	44
Pilot -3	19	3	4	26
Loader	15	2	3	20
Flagmen	4028	628	930	5586
Gr. Appl. -1	532	90	123	745
Gr. Appl. -2	16	3	4	23
Arizona Study				
Pilot -1	8	1	2	11
Pilot -2	90	15	21	176
Loader -1	1235	209	285	1729
Loader -2	46	8	11	65
Flagmen-1	5200	880	1200	7280
Flagmen -2	1950	330	450	2730

Table IV-12. Range of Dermal and Inhalation EPN Exposure to Applicators [a]

Personnel	High (ug)	Low(ug)	Inhalation[b]
Pilots	180	10	Negligible with Respirator
Loaders	1730	20	
Flaggers	7300	2700	
Ground Applicators	750	20	

[a] Assumes an 8 hour work day.

[b] To emphasize the importance of wearing a respirator the Agency points out that the following high/low inhalation exposures (ug) would occur in the event that a respirator is not worn: pilots, 10/10 loaders, 20/10; flaggers, 11500/10; ground applicators, 70/10.

Table IV-13. Summary of EPN Use Data[a]

Crop	Number of Workers Ground	 Aerial	 Loaders[b]	 Flaggers[c]
Cotton[d]	2385	523	2908	Not Quantified
Soybeans	1283	120	1403	
Corn (field)	NA	70	70	
Corn (sweet)	NA	72	72	
Pecans	590[e]	9	599	
Peaches	37[e]	1	38	
Tomatoes	1[f]	NA	1[f]	
Lettuce	1[f]	NA	1[f]	
Beans	1[e]/[f]	1[e]	2[f]	
Insecticide (Mosquitoes)[g]	NA	2	2	
TOTALS	4298	798	5096	

[a] From Memo dated 3/19/81 from Hoyt Jamerson (BFSD) to Patrick Miller (SPRD), EPN-Final Use Pattern Summary Report. (Memo, 1981a)

[b] Includes ground applicators.

[c] A quantitative estimate of the number of human flaggers working with EPN was not possible. Data from a recent NAAA survey indicates that use of human flaggers in aerial application of EPN is not uncommon, but does not represent standard practice (26% of aerial applicator respondents reported using human flaggers - the % of instances in which human flaggers were used was most often cited as 10% or less [EPA, 1981n]).

[d] The number of acre-treatments of EPN on cotton has declined approximately 53% (from 8,577,500 acre-treatments to 4,500,000 acre-treatments) since 1980 (Vlier, 1983). For purposed of this document the number of applicators applying EPN to cotton has been reduced proportionately.

[e] Application is by airblast equipment.

[f] Estimated -- No data given, but acreage is small, less than 300 for crops, except 3600 acres for beans.

[g] From Memo dated 9/19/80 from Hoyt Jamerson (BFSD) to Patrick Miller (SPRD), EPN-Final Use Pattern Summary Report. (Memo, 1980b)

Table IV-14. Applicator Exposure (Dermal) to EPN[a]

Workers	No.[b]	Hours/ day	Days/[c] year	ug per 8 hour work day Dermal[d] High	Low	Inhalation
Pilots	798	8	5-30	180	10	Negligible with respirator[f]
Loaders	5096[e]	8	5-30	1730	20	
Flaggers	Not quantified	-	-	7300	2700	
Ground Applicators	4298	8	1-12	750	20	
Bystanders		[No data for this group.]				

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[a] Assumes protective clothing according to label.

[b] Data from Table IV -13.

[c] Days per year of application varies with crop. Ranges specific to certain crops are as follows:

	Days/yr. pilots	Days/yr. Ground Applicators
Cotton	20-30	3-12
Soybeans	20-30	1-8
Field Corn	5-10	-
Sweet Corn	15	-
Pecans	-	3-6
Peaches	-	2-8

[d] Data from Table IV-12.

[e] This number duplicates some ground applicators because they perform both work functions.

[f] Respiratory exposure without respirators given in note to Table VI-12.

All parties involved in the EPN RPAR agree that, under certain experimental conditions, EPN has produced organophosphorus-type delayed neurotoxicity in chickens. However, identifying a NOEL for this effect, based on the chronic oral studies in chickens, is a major point of contention in assessing the risk to humans.[11/]

The ability of a compound to produce organophosphorus-type delayed neurotoxicity is considered to have been demonstrated when the syndrome described on page IV-1 of this chapter has been demonstrated to occur in a sensitive species at any dose or dose regimen. Identifying a NOEL then becomes a task of determining which of the signs indicative of this toxicity shall be used to distinguish between an effect dose and a no-effect dose. The signs of the neurotoxic effects are abnormal gait or ataxic gait and the histopathological determination of axonal destruction in the spinal cord.

The experimental studies available have raised the question as to whether abnormal gait or microscopically visible axonal damage is the most sensitive indicator of EPN

[11/] Because of inconsistencies in the available studies in chickens (different NOEL's reported) a single, precise NOEL for EPN-induced delayed neurotoxicity per se cannot reliably be determined.

neurotoxicity. There were originally four chronic oral dosing studies available which have produced data bearing on this question. One study, in which EPN was administered by capsules, reported abnormal gait at doses lower than those at which axonal lesions were observed (Abou-Donia and Graham, 1978). Two studies, in which EPN was administered in the feed, reported axonal lesions at doses lower than those at which abnormal gait was observed (Velsicol, 1979a; Nissan, 1979). The fourth study, also a feeding study, reported that abnormal gait and axonal lesions occurred simultaneously at the lowest positive doses (DuPont, 1979b). The Agency points out that three of these studies (Velsicol, 1979a; Nissan, 1979; DuPont, 1979b) were performed by Industrial Biotest Laboratories (IBT). Studies performed by IBT in support of pesticide registrations must be audited. All three of these studies have been reviewed. Two (DuPont, 1979b and Velsicol, 1979a) have been found to be valid; the other (Nissan, 1979) to be invalid. Table IV-15 shows the doses given and the effects reported in the above four studies.

As may be seen from Table IV-15, the observation of histopathological abnormalities appears to be consistent across the four studies. The effect is observed at 2.00 mg/kg per day in two studies and reported at all higher doses in all of the studies. The inconsistency is in the observations of abnormal gait. In the feeding studies, it is reported at doses of 3.00 mg/kg per day and higher, while in the capsule study at 0.1 mg/kg per day and higher. Also, two of the feeding studies report no gait abnormalities at a dose (2.00 mg/kg per day) at which they report histopathological lesions. These differences are critical, since the feeding studies give a NOEL of 1.00 mg/kg per day while the capsule study gives a NOEL of 0.01 mg/kg per day.

There are two possible reasons for this difference: 1) there is a real difference in effect between the types of studies, perhaps because of the ~~differences of~~ feeding and capsule administration, or 2) the observational systems and criteria differ significantly between laboratories. For this second possibility, the Agency points out that there were only two laboratories involved in these four studies. All three feeding studies were performed at one laboratory, Industrial Biotest, by the same staff, in the same facilities, and during the same general time period.

Table IV-15. EPN Neurotoxicity Studies in Chickens

Dose (ppm)	Nissan (1979) In Feed		DuPont (1979b) In Feed		Velsicol (1979a) In Feed		Abou-Donia & Graham (1978) Capsule		Dose (mg/kg)
	G	HP	G	HP	G	HP	G	HP	
0	0	0	0	0	0	0	0	0	0
	-	-	-	-	-	-	0	0	0.01
1	0	0	0	0	0	0	-	-	0.07a
	-	-	-	-	-	-	+	0	0.10
3	0	0	-	-	0	0	-	-	0.20
5	-	-	0	0	-	-	0	-	0.34
	-	-	-	-	-	-	+	0	0.50
10	0	0	-	-	0	0	-	-	0.67
15	-	-	0	0	-	-	+	0	1.00
30	0	+	-	-	0	+	-	-	2.00
	-	-	-	-	-	-	+	+	2.50
45	-	-	+	+	-	-	-	-	3.02
	-	-	-	-	-	-	+	+	5.00
100	+	+	-	-	+	+	-	-	6.70
	-	-	-	-	-	-	+	+	10.00

Symbols: "G" = gait
"HP" = histopathology
"-" = not done
"0" = no change
"+" = toxic effect.

a/ mg/kg equivalents of ppm were calculated using a conversion factor developed by Nissan from the body weight and food consumption data produced in their study: mg/kg = ppm X 0.067.

Thus, it appeared that the only real way to identify the cause of the differences between the two types of studies was to perform a fifth study at a totally different laboratory. After considering the extreme differences in observation in the capsule study, it was determined that simply re-running that study at another laboratory might be sufficient to resolve the discrepancies. Therefore, the three basic manufacturers of EPN chose to sponsor a repeat of the capsule study at Huntingdon Research Center. (The reported results of the Huntingdon Research Center Study (1982) are given in Section IV.A.2. of this chapter).

As may be seen from Table IV-4, the reported results of the Huntingdon Research Center study (1982) showed positive signs of ataxia occuring at 2.5 mg/kg and higher doses, and pathological changes occurring at 1.0 mg/kg and higher doses. The report of this study identified a NOEL for EPN of 0.5 mg/kg/day based on signs of neurotoxicity and histopathological examination of nerve tissue. However, as noted above, a review of the report by an Agency scientist considered 0.01 mg/kg/day a NOEL based on consideration of subtle histological changes observed in the spinal cord (Memo, 1983a). Thus, rather than clarifying the differences in NOEL's for EPN, the re-run of the capsule study appears to have only further clouded the issue.

A possible resolution of the NOEL problem was provided by the Moeller and Rider (1962) study of the effects of chronic low doses of EPN in humans. This is considered a very important study since it provides the only data in the species at risk. In Moeller and Rider, groups of five individuals each received EPN orally by capsule according to the following schedule:

3 mg/day for 32 days;
6 mg/day for 47 days; and
9 mg/day for 56 days.

No effects of any type were observed at doses of 3 and 6 mg/day. At 9 mg/day, depression of plasma and red blood cell (RBC) cholinesterase activity was observed but "no clinically manifested side effects were observed or reported."

This study of chronic oral administration to humans provides a NOEL of 6 mg/day, which is approximately equal to 0.1 mg/kg per day. The effects observed, depression of plasma and RBC cholinesterase activity, are the most sensitive indicators of EPN toxicity known.

Thus, a single NOEL for the delayed neurotoxic effect of EPN, based on the chronic oral studies in chickens, cannot reliably be determined. Even if the Huntingdon Research Center (1982) study represented the only data available for this effect of EPN there would be a problem in accepting a NOEL from this study because of the differences in interpretation presented above. To do so at this time would also ignore the Moeller and Rider (1962) data and the Abou-Donia (1978) study. Since there is no way of reconciling the various studies in the toxicology data base,* the Agency has used the available animal data and human data identifying a range of NOELs in calculating a margin of safety range.[12]

1. Dietary Exposure Risk Analysis

The Agency has identified NOELs for delayed neurotoxic effects of EPN ranging from 0.01 mg/kg/day to 1.0 mg/kg/day. Based on the "Probable Case" estimate of 4.4 x 10^{-5} mg/kg per day for a 70-kg individual given above in the dietary exposure analysis, an acceptable margin of safety (MOS) range (227 - 22,720[13] exists for dietary exposure of the general population to EPN residues on food (EPA,1981f).

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[12] The NOELs used in calculating ranges for margins of safety were: 0.01 mg/kg/day (Abou-Donia and Graham, 1978); 0.1 mg/kg/day (Moeller and Rider, 1962); 0.5 mg/kg/day (Huntingdon Research Center, 1982); and 1.0 mg/kg/day (Nissan, 1979; DuPont, 1979b; and Velsicol, 1979a).

[13] The MOS for each of the NOELs in the range is as follows:

NOEL	Exposure Estimate	MOS
0.01	4.4 x.10^{-5}	227
0.1	4.4 x 10^{-5}	2272
0.5	4.4 x 10^{-5}	11360
1.0	4.4 x 10^{-5}	22720

*Comments of former members of the Scientific Advisory Panel on this subject are contained in the EPN Federal Register Notice.

Based on the "Realistic Worst Case" estimate of 3.6×10^{-4} mg/kg per day for a 70 kg individual given above in the dietary exposure analysis, an acceptable margin of safety (MOS) range (27 - 2777)[14] exists.

Based on the "Worst Case" estimate of 1.2×10^{-2} mg/kg per day, if EPN were used on all acreage of all crops for which it is registered, the margin of safety range for delayed neurotoxicity, using the above NOEL range, would be 0.83 to 83.3.[15] The usually accepted margin of safety for delayed neurotoxicity is 100. An acceptable margin of safety does not exist in the "Worst Case" estimate.

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[14] The MOS for each of the NOELs in the range is as follows:

NOEL	Exposure Estimate	MOS
0.01	3.6×10^{-4}	27.0
0.1	3.6×10^{-4}	277.0
0.5	3.6×10^{-4}	1388.0
1.0	3.6×10^{-4}	2777.0

[15] The MOS for each of the NOELs in the range is as follows:

NOEL	Exposure Estimate	MOS
0.01	1.2×10^{-2}	0.83
0.1	1.2×10^{-2}	8.3
0.5	1.2×10^{-2}	41.6
1.0	1.2×10^{-2}	83.3

2. Application Exposure Risk Analysis

Based on data provided above in the applicator exposure analysis section, and a NOEL range of 0.01 mg/kg/day to 1.0 mg/kg/day for EPN, the Agency concludes that an adequate margin of safety during EPN application exists for pilots, loaders, and general applicators, under most but not all NOEL estimates, but an adequate margin of safety does not exist under any estimation for flaggers (EPA, 1981f).

Measurable applicator exposure to EPN is by the dermal, rather than inhalation route, provided that protective clothing and a respirator are worn. No direct data exist for determining the amount of dermal absorption of EPN. The solubility and physical state of EPN is such that a high rate of dermal absorption could be expected. Assuming a worst case of 100% dermal absorption, and based on the above NOEL range, the margins of safety ranges are 3.8 to 380 for pilots, 0.4 to 40 for loaders, 0.1 to 10 for flaggers, and 1 to 100 for ground applicators.[16/] The advantage to using

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[16/] The MOS for each of the NOELs in the range is as follows:

NOEL	Mos			
Exposure[a/] Estimate	Pilots (257 x 10-5)	Loaders (247 x 10-4)	Flaggers (104 x 10-3)	Ground Applicator (107 x 104)
1.0	380.0	40.0	10.0	100.0
0.5	190.0	20.0	5.0	50.0
0.1	38.0	4.0	1.0	10.0
0.01	3.8	0.4	0.1	1.0

[a/] The exposure estimate assumes the applicator to be a 70-kg individual a worst case approach as a first cut to evaluate applicator risk is that if the worst case shows no health hazard, then a refined determination of dermal absorption is not needed. However, in this case, margins of safety for most applicator groups would be considered unacceptable; a more refined approach is needed to determine what, if any, realistic risks exist for applicators.

The only information available to estimate a dermal absorption rate is the acute toxicity study by Gaines (1969). Gaines reported acute toxicity data from which apparent dermal absorption percentages of 16 in male rats and 31 in female rats can be calculated (see Table IV-16).

Using the 31% apparent dermal absorption, margins of safety ranges for the various applicator groups are 12.5 to 1250 for pilots, 1 to 100 for loaders, 0.3 to 33 for flaggers, and 3 to 303 for ground applicators.[17]

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[17] The MOS for each of the NOELs in the range is as follows:

NOEL Exposure[a] Estimate	MOS			
	Pilots (80×10^{-5})	Loaders (1×10^{-2})	Flaggers $(.03 \times 10^{-2})$	Ground Applicators (33×10^{-7})
1.0	1250.0	100.0	33.0	303.0
0.5	625.0	50.0	16.0	151.0
0.1	125.0	10.0	3.0	30.0
0.01	12.5	1.0	0.3	3.0

[a] The exposure estimate assumes the applicator to be a 70-kg individual.

Table IV-16. Acute Toxicity/Dermal Absorption of EPN in Rats

Species/Sex	Dose (mg/kg)		Apparent %
	Oral	Dermal	Dermal Absorption
Rat/Male	36.0	230.0	16
Rat/Female	7.7	25.0	31

Source: Gaines, 1969.

The margins of safety presented in footnote 17 are an expression of the uncertainty in identifying a "NOEL" for EPN. However, some of these NOELs are dependent upon more solid determinations of effects than others. Those effect levels in the studies which produced NOELs of 0.5 mg/kg and 1.0 mg/kg are clearly defined instances of delayed neurotoxicity. For these an MOS of at least 100 is considered necessary. Under this first criteria an adequate margin of safety does not exist for flaggers, nor can it exist under any other consideration. Pilots and ground applicators show an adequate margin of safety. The loaders present a border-line case, raising the question if 100 is adequate or if half that (50) is inadequate? There is no definitive answer to this question and risk/benefit judgements may be appropriate.

The NOEL of 0.1 mg/kg is based on a human study which produced depression of blood cholinesterase. Because of the mild nature of the effect and its demonstration directly in man, the species we are attempting to protect, a margin of safety of ten (10) is usually considered adequate. At this NOEL all except the flaggers are adequately protected.

The NOEL of 0.01 mg/kg, although for the serious effect of delayed neurotoxicity, is disputed in both studies. The observational sensitivity of Abou-Donia does not appear to be duplicable by other researchers. The effect reported appears very subtle and dependent upon the unique circumstances under which the studies were performed. The interpretation of the Huntingdon study which indicates a NOEL of 0.01 depends upon a shift in relative degrees of normality. The lowest margin of safety that would be accepted for any effect is 10 while the margin of safety for delayed neurotoxicity stated above is 100. Clearly the determination of adequacy under these circumstances needs another determinate, that is more information of another kind. The Agency will reassess and determine what type of information is needed in this area during development of the registration standard for EPN in FY 85.

A critical factor in O-P type neurotoxicity is the permanence of the effect. "Recovery", complete at low doses and partial at high, has been reported for all susceptible species. This has been attributed to either regrowth of damaged axons or compensation by the remaining functional neurons (a combination of these is also possible). It has been reported that the toxic lesion is first damage to the axon and then, with continual or higher chemical assult, damage to the cell body. Axons can regrow, nerve cells are not replaced.

If recovery is a compensating process then it would be impossible to conceive of any circumstances under which compounds producing O-P type delayed neurotoxicity could be safely utilized.

D. Comparative Risks of Alternative Pesticides to EPN

This section presents the Agency's analysis of the comparative risks (human and wildlife) for alternative pesticides to EPN. The analysis for each separate use of EPN: cotton, soybeans, field corn, sweet corn, pecans, peaches, mosquito larvicides, and other food uses. As a basis of comparison, readers should bear in mind the following: EPN's acute toxicity is considered to be high; EPN causes delayed neurotoxicity; a NOEL in humans of 0.1 mg/kg for cholinesterase inhibition has been established. Both oncogenicity and teratogenicity are data gaps for EPN. There is sufficient data to show that neither EPN nor p-nitrophenol are mutagenic. EPN, applied directly to water as a mosquito larvicide, is acutely toxic to fish; it is also very toxic to honeybees.

For purposes of qualitative comparison, alternative pesticides will be considered "similar" to EPN if the acute toxicities (oral, dermal, and inhalation) range from 0.1 to 10 times that of EPN's acute toxicity. The acute toxicities of alternative pesticides will be considered "less than" that of EPN if the toxicities are more than 10 times that of EPN. And the acute toxicities of alternative pesticides will be considered "more than" that of EPN if the toxicities are less than 0.1 times that of EPN. Table IV-17 lists the various toxicity parameters for EPN an its alternatives.

Table IV-17. Comparative Risks of Alternatives to EPN

	Human Risk								Wildlife Risk		
	Acute LD- or LC-50			Chronic Effects							
Chemical/Use	Oral	Dermal	Inhal.	Onco.	Muta.	Repro/Terata	Chron. Feed.	Del. Neuro.	Birds	Fish	Honeybees
EPN	7.8 and 33 mg/kg in M and F rats	25 and 230 mg/kg in F and M rats	102 mg/L in rat	data gap	No	data gap	NOEL of 150 ppm in M rat & 75 ppm in F rat	Yes; NOEL of 0.1 mg/kg (CNS inhibition in humans)	LD-50 of 3 mg/kg in mallard & 53.4 mg/kg in pheasant	96-hr LC-50 of 80 & 190 ppb in bluegill & rainbow trout	highly toxic; LD-50 contact toxicity <2 ug/bee
Acephate – cotton & soybeans	945 mg/kg in rat	2000 mg/kg in rat	no effect in rats at 1.81 mg/L	No	No	No	reduced weight & CNS at 100 & 300 ppm in rats	No	N/A	96-hr LC-50 of 1100 & >1000 ppm in rainbow trout & bluegill	highly toxic; LD-50 contact toxicity <2 ug/bee
Azinphos methyl – cotton, pecans & peaches	11 & 13 mg/kg in M & F rats	220 mg/kg in rat	range: 2000 to 20000 mg/L in rats	negative data only	N/A	No	No effect in rats up to 100 ppm; CNS decrease in dogs at 50 ppm & above	No	LD-50 of 136 mg/kg in mallard; 75 mg/kg in pheasant	96-hr LC-50 of 4.3 & 22 ppb in rainbow trout & bluegill	highly toxic; LD-50 contact toxicity <2 ug/bee
Carbaryl – soybeans, corn (field/sweet), pecans & peaches	850 mg/kg in M rat	>4000 mg/kg in rat, >2000 mg/kg in rabbit	N/A	data inconclusive	weak mutagen	data inconclusive	N/A	No	LD-50 of >2179 mg/kg in mallard; >2000 mg/kg in pheasant	96-hr LC-50 of 1950 & 6760 ppm in rainbow trout & bluegill	highly toxic; LD-50 contact toxicity <2 ug/bee
Carbofuran – field corn	7.1 mg/kg in rat	10,200 mg/kg in rabbit (10% G)	N/A	No	No	Oral NOEL for repro. effects of 10 ppm in rats; not teratogenic in rabbits up to 0.5 mg/kg/day	data gap	No	Oral LD-50 of 5.04 mg/kg in bobwhite; 4.15 mg/kg in pheasant; 0.397 mg/kg in mallard	96-hr LC-50 of 380 & 240 ppb in rainbow trout & bluegill	highly toxic; contact toxicity <2 ug/bee

Table IV-17. Comparative Risks of Alternatives to E/N (Cont.)

	Human Risk								Wildlife Risk		
	Acute LD- or LC-50			Chronic Effects							
Chemical/Use	Oral	Dermal	Inhal.	Onco.	Muta.	Repro/Terato	Chron. Feed.	Del. Neuro.	Birds	Fish	Honeybees
Endosulfan - peaches	43 mg/kg in M rat; 18 mg/kg in F rat	1650 mg/kg in F rabbit (tech.) & 182 mg/kg in F rabbit (90% tech.)	4-hr LC-50 0.35 mg/L in M rat; 0.08 mg/L in F rat	N/A	No	no repro. effects; [illegible] data - No teratogenic effects in rats at 0.5 & 1.5 mg/kg per day	1-yr study in mongrel dogs at 3, 10, & 30 ppm no significant effects noted	N/A	5-day LC-50 805 ppm in bobwhite; 1275 ppm in pheasant; 1053 ppm in mallard; oral LD-50 of 33 mg/kg in mallard	96-hr LC-50 2.75 ppb in bluegill; 28 ppb in rainbow trout (4% a.i. dust)	moderately toxic; contact toxicity 2 to 11 ug/bee
Fenthion - mosquito larvicide	100-615 mg/kg in rats	25-1250 mg/kg in rats	1-hr LC-50 2.4 mg/L in rat; 2 mg/L in mice	under review	data gap	single IP dose up to 150 mg/kg in rabbits - no effect; embryotox effects in mice at 40 mg/kg (IP); repro effects in rats at 60 ppm	100 ppm in diet suppressed ChE in rats; 50 ppm in diet no effect in beagles	No	LD-50 of 6 mg/kg in mallard; 17.8 mg/kg in pheasant	96-hr LC-50 0.84 ppm in rainbow trout; 0.93 & 1.38 ppm in rainbow trout & bluegill	highly toxic; contact toxicity <2 ug/bee
Fenvalerate - cotton	1-3 g/kg in rat; 450 mg/kg in rat	1-3 g/kg in rabbit	>53.3 mg/L in rat for 2.4 EC	No	No	No	NOEL of 250 ppm in rats; 100 ppm in mice	No	LC-50 of 10000 ppm in bobwhite & 5000 ppm in mallards	96-hr LC-50 of 1.2 & 0.63 ppb in rainbow trout & bluegill	highly toxic; LD-50 contact toxicity 0.41 ug/bee
Fonofos - field corn	3.16 - 17.5 mg/kg in rats	[illegible] 35 mg/kg in rabbits	1.2 mg/L in rat at 1-hr exposure to 10% dust	N/A	N/A	No	105-wk test in rats, ChE depression at 10 ppm - lowest dose - only at 19th & 26th wk in males	NOEL of 6.32 mg/kg per day in 46-day test in chickens	5-day LC-50 of 133 ppm in bobwhite, 1225 ppm in mallard	96-hr LC-50 of 0.05 ppm in rainbow trout; 0.029 ppm in bluegill	data gap

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Table IV-17. Comparative Risks of Alternatives to E/M (Cont.)

Chemical/Use	Human Risk Acute LD- or LC-50 Oral	Dermal	Inhal.	Chronic Effects Onco.	Muta.	Repro/Terato	Chron. Feed.	Del. Neuro.	Wildlife Risk Birds	Fish	Honeybees
Endosulfan - peaches	43 mg/kg in M rat; 18 mg/kg in F rat	1650 mg/kg in F rabbit (tech.) & 182 mg/kg in F rabbit (90% tech.)	4-hr LC-50 0.35 mg/L in M rat; 0.08 mg/L in F rat	N/A	No	no repro. effects; 1981 data - No teratogenic effects in rats at 0.5 & 1.5 mg/kg per day	1-yr study in mongrel dogs at 3, 10, & 30 ppm no signifi- cant effects noted	N/A	5-day LC-50 805 ppm in bobwhite; 1275 ppm in pheasant; 1053 ppm in mallard; oral LD-50 of 33 mg/kg in mallard	96-hr LC-50 2.75 ppb in bluegill; 28 ppb in rainbow trout (4% a.i. dust)	moderately toxic; contact toxicity 2 to 11 ug/bee
Fenthion - mosquito lar- vicide	100-615 mg/kg in rats	25-1250 mg/kg in rats	1-hr LC-50 2.4 mg/L in rat; 2 mg/L in mice	under re- view	data gap	single IP dose up to 150 mg/kg in rabbits - no effect; em- bryotox ef- fects in mice at 40 mg/kg (IP); repro ef- fects in rats at 60 ppm	100 ppm in diet sup- pressed ChE in rats; 50 ppm in diet no effect in beagles	No	LD-50 of 6 mg/kg in mallard; 17.8 mg/kg in pheasant	96-hr LC-50 0.84 ppm in rainbow trout; 0.93 & 1.38 ppm in rainbow trout & bluegill	highly toxic; contact toxicity <2 ug/bee
Fenvalerate - cotton	1-3 g/kg in rat; 450 mg/kg in rat	1-3 g/kg in rabbit	>3.3 mg/L in rat for 2.4 EC	No	No	No	NOEL of 250 ppm in rats; 100 ppm in mice	No	LC-50 of 10000 ppm in bobwhite & 5000 ppm in mallards	96-hr LC-50 of 1.2 & 0.63 ppb in rainbow trout & bluegill	highly toxic; LD-50 contact toxicity 0.41 ug/bee
Fonofos - field corn	3.16 - 17.5 mg/kg in rats	0 35 mg/kg in rab- bits	1.2 mg/L in rat at 1-hr expo- sure to 10% dust	N/A	N/A	No	105-wk test in rats, ChE depression at 10 ppm - lowest dose- only at 19th & 26th wk in males	NOEL of 6.32 mg/kg per day in 46-day test in chickens	5-day LC-50 of 133 ppm in bobwhite, 1225 ppm in mallard	96-hr LC-50 of 0.05 ppm in rainbow trout; 0.029 ppm in blue- gill	data gap

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Table IV-17. Comparative Risks of Alternatives to EPN (Cont.)

	Human Risk										
	Acute LD- or LC-50			Chronic Effects					Wildlife Risk		
Chemical/Use	Oral	Dermal	Inhal.	Onco.	Muta.	Repro/Terata	Chron. Feed.	Dol. Neuro.	Birds	Fish	Honeybees
Malathion - field corn	1375 mg/kg in M rat; 1000 mg/kg in F rat	>4444 mg/kg in M & F rat	>60 mg/L in M & F rat	neg. in rats & F mice; results equivocal in M mice	N/A	repro. effects in rat at 240 mg/kg; no terata in rat at 600 & 900 mg/kg via IM	N/A	N/A	5-day LC-50 3497 ppm in bobwhite; 4320 ppm in pheasant; >5000 ppm in mallard; LD-50 of 1485 mg/kg in mallard	96-hr LC-50 of 200 & 103 in rainbow trout & bluegill	highly toxic; contact toxicity <2 ug/bee
Methomyl - cotton, soybeans, sweet corn	15 - 27 mg/kg in rat	>1000 mg/kg in rat	0.39 - 0.51 mg/L	data gap	data gap	No	NOEL 100 ppm & 50 ppm in M & F rats; NOEL 100 ppm in dogs	No	oral LD-50 15.4 & 15.9 mg/kg in pheasant & mallard; LC-50 of 1100 ppm in bobwhite	96-hr LC-50 of 1600 & 1050 ppb in rainbow trout & bluegill	highly toxic; contact toxicity <2 ug/bee
Methyl parathion - cotton, soybean	6 - 18 mg/kg in M rat; 4.5 - 24 mg/kg in F rat	67 mg/kg in rat	4-hr 0.12 mg/L in M rat	data gap	No	repro. effect NOEL 10 ppm in rats	data gap	data gap	oral LD-50 of 8 mg/kg in pheasant; 10 mg/kg in mallard	LC-50 of 1.9 ppm in bluegill	highly toxic; contact toxicity <2 ug/bee
Monocrotophos - cotton	21 mg/kg in rat	112/126 mg/kg in F & M rat	No effect after 1-hr exposure to tech.	data gap	No	repro. effect NOEL 2 ppm in rats; not teratogenic	1 ppm NOEL in rats; 1.6 & 0.16 ppm NOEL in beagles	No	LC-50 of 3.1 ppm in pheasant; 9.6 & 32 ppm in 5- & 10-day old mallards	96-hr LC-50 4 & 4.9 ppm in bluegill & rainbow trout	highly toxic; contact toxicity <2 ug/bee

Table IV-17. Comparative Risks of Alternatives to EPN (Cont.)

	Human Risk								Wildlife Risk		
	Acute LD- or LC-50			Chronic Effects							
Chemical/Use	Oral	Dermal	Inhal.	Onco.	Muta.	Repro/Terata	Chron. Feed.	Del. Neuro.	Birds	Fish	Honeybees
Parathion - field & sweet corn, peaches, mosquito larvicide	2.04 - 30 mg/kg in M rat; 1.75 - 6 mg/kg in F rat	21 mg/kg in M rat; 6.8 - 100 mg/kg in F rat	0.0315 mg/L in M rat	data gap	Yes at 0.05 mg/kg in M guinea pigs	not teratogenic; repro effects at 3.0 & 3.5 mg/kg in rat	data gap	data gap	oral LD-50 of 2.13 mg/kg in mallard; 12.4 mg/kg in pheasant	96-hr LC-50 of 1430 & 400 ppb in rainbow trout & bluegill	highly toxic; contact toxicity <2 ug/bee. However, recent evidence suggests that permethrin may repel honeybees.
Penncap M - sweet corn, peaches	The Agency assumes that Penncap M (encapsulated methyl parathion) has the same toxicity as methyl parathion (see above). However, the Agency also has substantive data which indicate that Penncap M is much more toxic to bees than conventional methyl parathion.										
Permethrin - cotton	3 g/kg in rat	>2 g/kg in rabbit	>215 mg/L in rat (4 hrs)	Studies under review	No	No	NOEL of 20 ppm in rats	NOEL of 2500 ppm	LC-50 of >10000 ppm for both mallards & bobwhite; oral LD-50 >4640 mg/kg in mallards	96-hr LC-50 of 2.5 ppb in bluegill	highly toxic; contact toxicity 0.05 ug/bee
Phorate - field corn	1.75 - 3.66 mg/kg in M rat	415 mg/kg in guinea pig; 71 mg/kg in rabbit; 3 mg/kg in M rat	no mortality at 8 hrs in rat	data gap	data gap	terata - data gap; NOEL for repro. effects in mice of 1.5 ppm	data gap	No effect at 40 ppm	LD-50 of 0.616 mg/kg in mallard; 7.12 mg/kg in pheasant	96-hr LC-50 of 13 & 20 ppb in rainbow trout (100% a.i.) & bluegill (91% a.i.)	moderately toxic; contact toxicity 2 - 11 ug/bee
Phosalone - pecans	125 mg/kg in M rat; 90 mg/kg in F rat; 120 mg/kg in M & F rat	1530 mg/kg in F rat; >1000 mg/kg in rabbit	data gap	No	No	No	No effects except CNS effects up to 250 ppm in rats	No	data gap	96-hr LC-50 of 0.92 ppm in rainbow trout & "highly toxic" to bluegill (34.87% a.i.)	moderately toxic; contact toxicity 2 to 11 ug/bee

Table IV-17. Comparative Risks of Alternatives to EPN (Cont.)

	Human Risk								Wildlife Risk		
	Acute LD- or LC-50			Chronic Effects							
Chemical/Use	Oral	Dermal	Inhal.	Onco.	Muta.	Repro/Terata	Chron. Feed.	Del. Neuro.	Birds	Fish	Honeybees
Phosmet - peaches	113 - 310 mg/kg in rat	1500 - 3160 mg/kg in rat; 3160 - 4640 in rabbit	1-hr LC-50 >7.35 mg/L in rat (5% dust)	data gap	Negative Ames test; some cytogenicity in mice	No	40 ppm NOEL in rats; 40 ppm NOEL in beagles	No	5-day LC-50 501 ppm in bobwhite; 3146 ppm in pheasant; >5000 ppm in mallard	96-hr LC-50 of 0.56 ppm in bluegill; 0.145 ppm in rainbow trout	highly toxic; contact toxicity 1.06 ug/bee
Sulprofos - cotton	262 mg/kg in M rat; 275 mg/kg in F rat	>1000 mg/kg in rat; 820 mg/kg in M rabbit; 994 mg/kg in F rabbit	>0.5 mg/L (all species tested)	No	Data gap	No	No	No	LC-50 of 99 ppm in bobwhite; 983 ppm in mallards	96-hr LC-50 of 2.5 ppb in bluegill	highly toxic; contact toxicity 0.05 ug/bee
Temephos - mosquito larvicide	2030 mg/kg in M rat; 2330 mg/kg in F rat	1930 mg/kg in M rabbit; 970 mg/kg in F rabbit	No sign of toxicity in rats after 1 hr exposure in nearly saturated air	No	N/A	No repro effects in rats up to 125 ppm	No effect except increased liver weight in rats at 10, 100, & 300 ppm	No effect at 900 ppm (single dose)	N/A	96-hr LC-50 of 1 ppm in rainbow trout; 21.8 ppm in bluegill	moderately toxic; contact toxicity 2 to 11 ug/bee
Toxaphene - soybeans	90 mg/kg in M rat; 80 mg/kg in F rat	1075 mg/kg in M rat; 780 mg/kg in F rat	N/A	Yes	Yes	possible repro effect additional testing needed	No chronic effects other than mutagenicity	N/A	LD-50 of 70.7 mg/kg in mallard; 40 mg/kg in pheasant; 40 mg/kg in bobwhite	96-hr LC-50 2.4 - 18 ppb in bluegill; 1.8 - 11 ppb in rainbow trout	relatively nontoxic; contact toxicity above 11 ug/bee

[Additional data on the toxicity of these alternatives to wildlife was taken from Johnson and Finley (1980); Tucker and Crabtree (1970); and Hill et al. (1975).]

1. Cotton

The following chemicals have been analyzed as alternatives to use of EPN on cotton: acephate, azinphos-methyl, fenvalerate, methomyl, methyl parathion, monocrotophos, permethrin, and sulprofos.

°Acephate—is less acutely toxic than EPN. It does not cause delayed neurotoxicity. There are data showing that acephate is not teratogenic, oncogenic, or mutagenic (EPA 1981h).

°Azinphos-methyl—is similar to the acute oral and dermal toxicities of EPN. It is less toxic via inhalation. It does not cause delayed neurotoxicity. There are data showing that azinphos-methyl is not oncogenic, but there are data which show reproductive effects in rats (reduced pup weight and weanling survival) at 5 mg/kg. Humans exposed at 9 mg/kg per day showed no depression of plasma or RB cholinesterase activity (EPA 1980g). It has been associated with reports of numerous fish kills in the field (EPA 1980h). It is highly toxic to honeybees (Atkins et al. 1976).

°Fenvalerate—is less acutely toxic than EPN orally and dermally. It is more toxic via inhalation. There are data showing that fenvalerate is not oncogenic, mutagenic, or teratogenic. Delayed neurotoxicity is a data gap (EPA 1980g). Fenvalerate is highly toxic to bees; it is extremely toxic to fish and aquatic invertebrates (EPA 1980h).

°Methomyl—is similar to the acute oral and dermal toxicities of EPN. It is more toxic via inhalation. There are data showing that methomyl is not a delayed neurotoxin or teratogen. Oncogenicity is a data gap (EPA 1980g). Methomyl does not appear to be toxic to birds or mammals under field conditions (EPA 1980h). It is highly toxic to honeybees (Atkins et al. 1976).

°Methyl parathion—is similar to the acute oral and dermal toxicities of EPN. It is more via inhalation. There are data showing reproductive effects in rats at 10 and 30 ppm in the diet. There are data showing that methyl paration is not mutagenic. Humans exposed at 20 mg/kg per day for 4 weeks showed no decrease in plasma or RB cholinesterase activity (EPA 1980g). An application of 1 pound directly to six inches of water would not be acutely toxic to the most sensitive fish species (bluegill). The LD-50 in Daphnia is 114 ppb [EPA 1980h]. It is highly toxic to honeybees (Atkins et al. 1976).

°Monocrotophos--is similar to the acute oral and dermal toxicities of EPN. It is less toxic via inhalation. There are data showing that monocrotophos has not been shown to be teratogenic. There are some data which suggest it may be mutagenic (EPA 1980g). Monocrotophos has a half-life of 100 days and is about 10 times as toxic a EPN (96-hr LC_{50}) to bluegill and is highly toxic to birds (EPA 1980h). It is also highly toxic to honeybees (Atkins et al. 1976).

°Permethrin--is less acutely toxic than EPN orally and dermally. It is similar to the acute inhalation toxicity of EPN. Data on the oncogenicity remain to be reviewed by the Agency. There are data showing that paramethrin is not a teratogen, or mutagen. In two separate 3-generation reproductive studies in rats, NOELs of 100 ppm and less than 500 ppm were established. Permethrin has shown neuropathologic effects, with a NOEL of 2500 ppm in both short- and long-term studies (EPA 1980g). Permethrin is much more toxic to aquatic organism than EPN; it is also highly toxic to honeybees (EPA 1980h).

°Sulprofos--is similar to the acute oral and dermal toxicities of EPN. It is more toxic via inhalation. There are data showing that sulprofos does not present oncogenic, teratogenic, or other reproductive risks. There is a data gap in the area of mutagenicity. It does not cause delayed neurotoxicity. An ADI, based on ChE inhibition, of 0.25 mg/kg per day has been established. Sulprofos is acutely toxic to honeybees (EPA 1981h).

2. Soybeans

The following chemicals have been analyzed as alternatives to use of EPN on soybeans: acephate, carbaryl, methomyl, methyl parathion, and a toxaphene/methyl parathion combination.

°Acephate—see discussion under "Cotton" above.

°Carbaryl—is less acutely toxic than EPN orally and dermally (Martin 1972). Data indicate that carbaryl does not pose a human teratogenic or reproductive hazard under proper environmental usage. Carbaryl is a weak mutagen in test systems. Data from tests for oncogenicity are inconclusive. It is not a delayed neurotoxin (EPA 1980j). Carbaryl is highly toxic to honeybees (Atkins et al. 1976).

°Methomyl—see discussion under "Cotton" above.

°Methyl parathion—see discussion under "Cotton" above.

°Toxaphene (in combination with methyl parathion)—see discussion under "Cotton" above for methyl parathion. Toxaphene has been cancelled. It is similar to the acute oral and dermal toxicity of EPN (Martin 1972).

Position Document 1, issued in May 1977, was based on data showing that toxaphene was oncogenic, resulted in other chronic and/or delayed toxic effects, was acutely toxic to aquatic organisms, and caused population reductions in nontarget organisms. Data indicate that toxaphene is a mutagen. It is more toxic to aquatic organisms than EPN (EPA 1977a). It is relatively nontoxic to honeybees (Atkins et al. 1976).

3. Field Corn

The following chemicals have been analyzed as alternatives to use of EPN on field corn: carbaryl, carbofuran, fonofos, malathion, parathion, and phorate.

°Carbaryl--see discussion under "Soybeans" above.

°Carbofuran--is similar to the acute oral toxicity of EPN. It is less toxic dermally. There are data which indicate that carbofuran is not oncogenic, mutagenic, teratogenic, or neurotoxic. Several tests for reproductive effects in rats established a dietary NOEL of 10 ppm (EPA 1980g). Carbofuran appears to be less acutely toxic to aquatic organisms than EPN (EPA 1980h). It is highly toxic to honeybees (Atkins et. al. 1976).

°Fonofos--is similar to the acute oral and dermal toxicity of EPN. It is more toxic via inhalation. There are data showing that fonofos is not teratogenic and does not cause reproductive effects. A NOEL of 6.32 mg/kg per day has been established for neurotoxicity. Fonofos is similar to EPN's toxicity to birds, but is more toxic to fish. No data are available on its toxicity to honeybees (EPA 1975a).

°Malathion—is less acutely toxic than EPN orally and dermally. It is similar to EPN via inhalation. There are data which show that malathion is not teratogenic in rats. NCI recently completed a bioassay of malathion in rats and mice. NCI reported negative results for oncogenicity in both species. Analysis of the data for male mice, using several statistical methods, were equivocal. The Agency considers that further testing in male mice may be required. Malathion is about as acutely toxic to fish as EPN. Malathion is highly toxic to honeybees (EPA 1975b; Atkins et al. 1976).

°Parathion—is similar to the acute oral and dermal toxicity of EPN. It is more toxic via inhalation. Although parathion does not appear to be teratogenic, it does cause reproductive effects in rats, including decreased fetus weight, increased resorptions, reduced number of fetuses, and increased stillbirths and neonatal death. Oncogenicity and neurotoxicity are data gaps (EPA 1980g). Parathion is more acutely toxic to fish than EPN (EPA 1980h) and is highly toxic to honeybees (Atkins et al. 1976).

°Phorate--is similar to the acute oral and dermal toxicity of EPN. It is less toxic via inhalation. A 3-generation reproductive effect test in mice established a NOEL of 1.5 ppm. Oncogenicity, mutagenicity, and teratogenicity are data gaps (EPA 1981g). It is moderately toxic to honeybees (Atkins et al. 1976).

4. Sweet Corn

The following chemicals have been analyzed as alternatives to use of EPN on sweet corn: carbaryl, a carbaryl/parathion combination, methomyl, parathion, and Penncap M^R (encapsulated methyl parathion).

°Carbaryl--see discussion under "Soybeans" above.

°Carbaryl/parathion--see discussion under "Soybeans" (for carbaryl) and under "Field Corn" (for parathion) above.

°Methomyl--see discussion under "Cotton" above.

°Parathion--see discussion under "Field Corn" above.

°Penncap M^R--is a special flowable microencapsulated formulation of methyl parathion. Encapsulated pesticides are enclosed in tiny capsules (or beads) of thin polyvinyl or other plastic material to control release of the chemical and extend the period of diffusion (Meister 1981). Lacking data to the contrary, the Agency will assume that there is no significant difference between the toxicity of Penncap M^R

and methyl parathion. The Agency has substantial data, however, which indicate that the bee hazard of Penncap M^R is much greater than that of conventional methyl parathion. See discussion of methyl parathion under "Cotton" above.

5. Pecans

The following chemicals have been analyzed as alternatives to use of EPN on pecans: azinphos-methyl, carbaryl, dialifor, dimethoate, disulfoton, and phosalone.

°Azinphos-methyl--see discussion under "Cotton" above.

°Carbaryl--see discussion under "Soybeans" above.

°Dialifor--all the areas of acute and chronic toxicity for dialifor are data gaps, either because data are not available, or because the available data are invalid or not-yet-validated IBT data. Testing is being required on the acute and chronic toxicity of dialifor under the Registration Standard program. If the not-yet-validated acute oral and dermal toxicity IBT data for dialifor are found to be valid, then dialifor's acute oral and dermal toxicity could be characterized as similar to that of EPN (EPA 1981i). It is relatively nontoxic to honeybees (Atkins et al. 1976).

°Dimethoate--is less acutely toxic than EPN. The conclusion of the dimethoate RPAR indicated that the evidence for dimethoate's oncogenicity is only suggestive; registrants are being required to perform further testing. Mutagenicity risk is low. An NOEL of 2.8 mg/kg per day has been determined for teratogenic effects. The most probable margin of safety (MOS) for teratogenicity for general population (i.e., dietary) exposure is 875; the MOS for teratogenicity for dimethoate applicators varies by crop, formulation type, and appliation method. Ground air blast application and dust formulations generally pose unreasonable risk (MOS = 7 to 23). There is not enough evidence to determine whether dimethoate causes delayed neurotoxicity; additional testing is being required. Dimethoate is less toxic to aquatic organisms than EPN (EPA 1980i). It is highly toxic to honeybees (Atkins et al. 1976).

°Disulfoton--is similar to the acute oral and dermal toxicity of EPN (Martin 1972). Chronic testing is being required under the "Data Call-in Program." It is moderately toxic to honeybees (Atkins et al. 1976).

°Phosalone--is similar to the acute oral and dermal toxicity of EPN. Inhalation toxicity is a data gap. There are data showing that phosalone is not oncogenic, mutagenic, or teratogenic; an that it does not cause reproductive or delayed neurotoxic effects. It is moderately toxic to honeybees (Atkins et al. 1976).

6. Peaches

The following chemicals have been analyzed as alternatives to use of EPN on peaches: azinphos methyl, carbaryl, endosulfan, parathion, Penncap M, and phosmet.

°Azinphos methyl--see discussion under "Cotton" above.

°Carbaryl--see discussion under "Soybeans" above.

°Endosulfan--is less acutely toxic than EPN. there are data which indicate that endosulfan is not mutagenic or teratogenic. No reproductive effects were observed in rats given up to 50 ppm in the diet (EPA 1980g). Endosulfan is more acutely toxic to aquatic organisms than EPN (EPA 1980h). It is moderately toxic to honeybees (Atkins et al. 1976).

°Parathion--see discussion under "Field corn" above.

°Penncap M^{R}--see discussion under "Sweet corn" above.

°Phosmet--is similar to the acute oral and inhalation toxicity of EPN. It is less toxic dermally. Oncogenicity is a data gap. There are data showing that phosmet is not teratogenic, and does not cause delayed neurotoxic or reproductive effects. For mutagencity, phosmet has shown negative results in the Ames test, and slight cytogenicity in mice. Phosmet is less toxic to birds and fish than EPN. It is highly toxic to honeybees (EPA 1977b).

7. Mosquito Larvicides

The following chemicals have been analyzed (EPA 1980h) as alternatives to use of EPN as a mosquito larvicide: chlorpyrifos, fenthion, parathion, and temephos. EPN use as a mosquito larvicide exceeds the risk criterion for acute toxicity to aquatic organisms. The analysis of alternative pesticides for this use will therefore consider only their effect on aquatic organisms when the alternatives are used as mosquito larvicides.

° Chlorpyrifos--The acute exposures posed by the mosquito control use pattern to aquatic organisms greatly exceed the RPAR risk criterion, i.e., when used according to label directions, the concentration in a 6-inch layer of water exceeds 1/2 the acute LC_{50} for representative species likely to be exposed.

°Fenthion--The mosquito control use pattern presents low to moderate risks to aquatic invertebrates. Fish do not appear to be directly at risk from use, but may be indirectly affected if invertebrate food organisms are killed by fenthion's use for mosquito control. (Referred to EPA by FDA on the basis of oncogenicity)

°Parathion--0.1 pounds a.i. applied to a 6-inch layer of water would result in a residue of 73.4 ppb. LC_{50} values range from about 50 ppb for bluegill to 2.5 ppm for minnows. Deformities were observed in bluegills exposed for 23 months to 0.34 ug/liter (= ppb); tremors, convulsions, hypersensitivity, and hemorrhages were observed at higher concentrations. Parathion used as a mosquito larvicide is more toxic than EPN.

°Temephos—0.2 pounds a.i. (granular formulation) applied to a 6-inch layer of water would result in residues ot 147 ppb. The 96-hour LC_{50} for rainbow trout exposed to technical temephos is 1.0 ppm. (The Agency has data which show that the 43% a.i. EC product is about 20X more toxic to fish than the technical.) The use of temephos for mosquito control is virtually harmless to most aquatic organisms, though some invertebrates might be adversely affected.

V. BENEFIT ANALYSIS OF EPN

In this chapter, the Agency examines the following issues: 1) the expected use under continued registration of EPN on cotton, field corn, soybeans, peaches, pecans, sweet corn, miscellaneous vegetables (lettuce, beans, tomatoes), and on aquatic areas for mosquito control; 2) the costs of alternative treatment programs; and 3) the projected economic impact on agricultural producers, consumers, and the economy as a whole should EPN be cancelled.

A. Introduction

EPN is registered for use as a broad spectrum insecticide and acaricide on a large number of agricultural crops and for ground and aerial application as a mosquito larvicide. Although registered for use on numerous agricultural crops, EPN is used mainly on cotton, field corn, sweet corn, and soybeans. EPN's use on other food crops is negligible (EPA, 1979a; Memo, 1979).

The Agency depended upon a team of agricultural specialists from the USDA and EPA (the EPN Biological Assessment Team) to compile and evaluate background data of an agronomic or entomological nature (USDA-EPA-States, 1980). This preliminary work, as well as various RPAR rebuttal responses, served as the basis upon which the "EPN

Benefit Analysis " was subsequently developed (EPA, 1981j). With regard to the latter report, the Agency relied heavily upon the efforts of cooperating universities for gathering and evaluating additional data, and in some cases, for drafting analyses.

Where data generated by either the Assessment Team or the Agency's University cooperators were incomplete, recourse was made to the informed opinions of various local agricultural experts. Based upon an analysis of all foregoing data in 1981 the Agency estimated the impacts that would result from the cancellation of EPN (EPA, 1981j). Due to substantial changes in the cotton insecticide market, the cotton portion of the 1981 analysis was revised in 1983 (Vlier, 1983). Economic impacts, where quantified, are in 1980 dollars with the exception of the cotton impacts which are reported in 1982 dollars.

B. Cotton

Approximately 13 million acres of cotton are harvested annually in the United States (1979-1981 average) (USDA, ERS, 1981). While cotton is grown in eighteen southern and western states,[18/] production in recent times has become predominately localized in three areas: 1) in Arkansas,

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18/ Cotton is grown in the following states: AL, AZ, AR, CA, FL, GA, KY, LA, MS, MO, NV, NM, NC, OK, SC, TN, TX, and VA.

Louisiana, and Mississippi in the Delta Region; 2) in Oklahoma and Texas in the South west; and 3) in California and Arizona in the West. The bulk of EPN use on cotton is concentrated in the Delta Region.

1. Use of EPN and Alternatives

EPN and combinations thereof with other chemicals are registered for use on cotton, primarily targeting Heliothis zea (bollworm), Heliothis virescens (tobacco budworm), and Anthonomus grandis (boll weevil). Therefore, the alternatives to EPN or its combinations are insecticides registered for the control of at least one of the foregoing pests.

While several different formulations of EPN are available, the one used predominantly is a combination of EPN and methyl parathion (EPN/MP) containing 3 pounds of each active ingredient each per gallon of formulated product. In the absence of data regarding the relative market shares of the various formulations, an assumption that all cotton producers use the EPN/MP 3-3 formulation has been made for analytical purposes. Although the application rate recommended by the various state extension services ranges from 0.25 to 1.0 pound of active ingredient per acre, the more commonly used rate ranges from 0.50 to 0.75 pound per acre.

Developed as early as 1949, EPN was little used as a cotton insecticide until the mid-1970's. It would appear that usage peaked in 1977 at 11.1 million pounds of active ingredient, dropped sharply in 1978 to 3.8 million pounds active ingredient and has continued to decline through 1982 (Vlier, 1983). Between 1979 and 1982 annual EPN usage on cotton has ranged from 1.5 to 2.7 million pounds active ingredient (Vlier, 1983).[19] During the 1970's the fluctuations in usage were largely in response to the ups and downs of *Heliothis* infestations. However, declines in EPN use since 1979 have occurred in response to the introduction of the synthetic pyrethroids, fenvalerate and permethrin, to the cotton insecticide market.

The original 1981 analysis (EPA, 1981j) estimate of EPN benefits on cotton was based on 1980 projections of EPN usage and 1980 cotton insecticide prices. The dominance of the synthetic pyrethroids in the cotton insecticide market of the early 1980's was not reflected in the 1980 projections. Thus, the cotton benefit analysis was updated in 1983 to reflect 1982 prices and 1979-1982 EPN usage levels.

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[19] Assumes an average dosage of 0.6 pounds of EPN active ingredient per acre.

Available information indicates that, as in the past, EPN is used almost exclusively for early season treatment in those areas which are infested with both Heliothis spp. and boll weevil. EPN use is largely concentrated in the Delta area of cotton production, although it is also applied in Texas and Southeastern cotton areas.

2. Comparative Efficacy: EPN vs. Alternatives

In general, it can be stated that several alternatives are at least as effective as EPN/MP in controlling Heliothis spp. on a season-long basis. In the 1981 analysis, this proposition was tested statistically by pooling various field trials comparing the efficacy (in terms of both cotton yield and insect damage) among EPN/MP or EPN and five alternatives: permethrin, fenvalerate, acephate, sulprofos, and methomyl.

When EPN/MP was compared with the five above-noted alternatives taken as a group, the null hypothesis of equal yields was rejected at the 0.005 level of significance in a single tailed test. This rejection leads to the acceptance of (but does not "prove") the alternative hypothesis that the alternatives are more effective than EPN/MP. However, when the latter was tested against the various alternatives on an individual basis, the null hypothesis (i.e., no difference in yields) was rejected only for fenvalerate and permethrin. Thus, it would appear that the superior efficacy of the two synthetic pyrethroids "carried" the remaining alternatives in the grouped efficacy comparison.

In this regard it should be acknowledged that the efficacy of the synthetic pyrethroids might not continue indefinitely. Laboratory testing has raised the possibility of eventual resistance. However, the Agency has not found documentation that resistance problems have been encountered outside the laboratory, and predictions in this regard would be merely speculative. Likewise, considerable uncertainty surrounds the question whether resistance problems in general can be combatted by alternating pesticides, since cross-resistance is common. Given this uncertainty, and given the absence of actual resistance problems as yet encountered with pyrethroids in the field, any projections about the possible role of EPN in efforts to combat resistance to pyrethroids would also be speculative.

The foregoing conclusion, drawn from the 1981 analysis, that the pyrethroids are more efficacious than EPN/MP, is based upon trials consisting of season-long treatments. However, although EPN/MP is used mainly for early-season treatments, it can be safely concluded that the cancellation of EPN would result in little yield effect on cotton production.

3. Comparative Cost: EPN vs. Alternatives

For the evaluation of relative treatment costs, a simplistic application-for-application comparison on a per-acre basis for EPN/MP vs. alternatives is not appropriate. Implicit in such comparison is the assumption that the residual control of the respective chemicals is identical. In reality this is not the case. Therefore, a more meaningful comparison is engendered by calculating the daily unit control costs, whereby the costs per acre-treatment are divided by the commonly observed treatment intervals.

The practice of following a fixed treatment schedule has been rendered obsolete by a combination of economic and educational factors. For the most part, producers no longer treat preventively, but rather on an as-needed basis, such treatment being triggered by the attainment of a predetermined economic threshold level of pest infestation. Thus the treatment interval, as used here, refers to the time lapse between sprays that are commonly followed once the threshold level has been reached. As with any abstraction, the concept of a neatly defined treatment interval is a simplification of what actually occurs in the field.

Based on the data presented in Table V-1 and V-2, it can be concluded that EPN/MP is generally more expensive on an average daily basis than the synthetic pyrethroids - fenvalerate and permethrin.

Table V-1. Average Daily Insecticidal Costs Per Acre-Treatment for Control of *Heliothis* with EPN/MP and Alternatives at Various Application Rates and Treatment Intervals

Insecticide	Dosage a/ (lbs. a.i./acre)	Common Treatment Interval a/ (Days)	Cost Per Acre-Treatment Per Day b/ ($)	Rank in Terms of Least Cost	Cost Per Acre-Treatment Per Day c/ ($)	Rank in Terms of Least Cost	Cost Per Acre Acre-Treatment Per Day d/ ($)	Rank in Terms of Least Cost
	Minimum Rate							
EPN/MP	0.50 + 0.50	6	0.69	3	0.75	3	0.88	3
Fenvalerate	0.10	10	0.60	1	0.64	1	0.71	1
Permethrin	0.10	10	0.60	1	0.64	1	0.71	1
Sulprofos	0.75	7	0.80	4	0.86	4	0.97	4
Acephate	0.75	7	1.12	5	1.17	5	1.28	5
Methomyl	0.45	6	1.23	6	1.30	6	1.43	6
	Intermediate Rate							
EPN/MP	0.60 + 0.60	5	0.93	1	1.01	1	1.16	3
Fenvalerate	0.12	7	0.99	3	1.04	2	1.15	1
Permethrin	0.12	7	0.98	2	1.04	2	1.15	1
Sulprofos	1.00	5	1.41	4	1.49	4	1.64	4
Acephate	1.00	4	2.49	6	2.59	6	2.78	6
Methomyl	0.45	5	1.48	5	1.56	5	1.71	5
	Maximum Rate							
EPN/MP	1.00 + 1.00	4	1.72	3	1.82	3	2.01	3
Fenvalerate	0.20	7	1.52	2	1.57	1	1.68	1
Permethrin	0.20	7	1.51	1	1.57	1	1.68	1
Sulprofos	1.50	5	1.98	4	2.05	4	2.20	4
Acephate	1.00	4	2.49	6	2.59	6	2.78	6
Methomyl	0.67	5	2.07	5	2.15	5	2.30	5

a/ From the 1981 EPN Cotton Benefit Analysis.
b/ 1982 chemical cost per acre-treatment plus an aerial application charge of $1.35 per acre-treatment divided by the common treatment interval.
c/ 1982 chemical cost per acre-treatment plus an aerial application charge of $1.75 per acre-treatment divided by the common treatment interval.
d/ 1982 chemical cost per acre-treatment plus an aerial application charge of $2.50 per acre-treatment divided by the common treatment interval

Source: Vller, 1983.

Table V-2. Average Daily Insecticidal Costs Per Acre-Treatment for Control of Heliothis and Boll Weevil with EPN/MP and Alternatives at Various Application Rates and Treatment Intervals

Insecticide	Dosage [c] (lbs. a.i./acre)	Common Treatment Interval [c] (Days)	Cost Per Acre-Treatment Per Day [d] ($)	Rank In Terms of Least Cost	Cost Per Acre-Treatment Per Day [e] ($)	Rank In Terms of Least Cost	Cost Per Acre Acre-Treatment Per Day [f] ($)	Rank In Terms of Least Cost
	Minimum Rate							
EPN/MP	0.50 + 0.50	4	1.03	3	1.13	3	1.32	3
Fenvalerate + MP[a]	0.10 + 0.25	4+4	1.00	2	1.09	1	1.28	1
Permethrin + MP[a]	0.10 + 0.25	4+4	0.99	1	1.09	1	1.28	1
Methomyl + MP[b]	0.45 + 0.25	4	2.01	5	2.11	5	2.30	5
Sulprofos + MP[b]	0.75 + 0.25	4	1.56	4	1.65	4	1.85	4
Acephate + MP[b]	0.75 + 0.25	4	2.11	6	2.21	6	2.40	6
	Intermediate Rate							
EPN/MP	0.60 + 0.60	4	1.17	3	1.27	3	1.46	3
Fenvalerate + MP[a]	0.12 + 0.25	4+4	1.11	1	1.21	1	1.40	1
Permethrin + MP[a]	0.12 + 0.25	4+4	1.11	1.	1.21	1	1.40	1
Methomyl + MP[b]	0.45 + 0.25	4	2.01	5	2.11	5	2.30	5
Sulprofos + MP[b]	0.00 + 0.25	4	1.92	4	2.01	4	2.20	4
Acephate + MP[b]	1.00 + 0.25	4	2.65	6	2.75	6	2.94	6
	Maximum Rate							
EPN/MP	1.00 + 1.00	3	2.29	3	2.63	3	2.68	3
Fenvalerate + MP[a]	0.20 + 0.25	4+3	1.80	2	1.91	1	2.13	2
Permethrin + MP[a]	0.20 + 0.25	4+3	1.79	1	1.91	1	2.12	1
Methomyl + MP[b]	0.67 + 0.25	4	2.75	6	2.85	6	3.04	6
Sulprofos + MP[b]	1.50 + 0.25	4	2.63	4	2.72	4	2.91	4
Acephate + MP[b]	1.00 + 0.25	4	2.65	5	2.75	5	2.94	5

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[a] Separate application of methyl parathion

[b] Tank mix.

[c] From the 1981 EPN Cotton Benefit Analysis.

[d] 1982 chelcal cost per acre-treatement plus an aerial application charge of $1.35 per acre-treatment divided by the common treatment interval.

[e] 1982 chemicl cost per acre-treatment plus an aerial application charge of $1.75 per acre-treatment divided by the common treatment interval.

[f] 1982 chemical cost per acre-treatment plus an aerial application charge of $2.50 per acre-treatment divided by the common treatment interval.

Source: Vilor, 1983.

4. Economic Impacts Due to Cancellation of EPN: User Impacts

Since the volume of EPN applied to cotton has significantly declined since the late 1970's, and the relative costs of EPN and alternative insecticides have shifted to favor the synthetic pyrethroids, the economic impacts of an EPN cancellation on cotton are minimal. Given the agronomic and entomologic data developed for the 1981 EPN cotton Benefit Analysis, the synthetic pyrethroids are equally efficacious to and more persistent than EPN/MP. Maximum EPN benefits would only be $175,000 annually and would only occur if it is assumed that 3.5 million acre-treatments of EPN/MP were applied in a normal year, and that all treatments were made with intermediate *Heliothis* infestations.

Although aggregate impacts are anticipated to be small, some individual growers may experience substantial benefits from the application of EPN to cotton. This would be true in areas where treatment intervals differ from those assumed in the analysis and/or EPN is more useful in controlling secondary cotton pests.

5. Limitation of Analysis

The primary limitation of the analysis is the reliance on estimated treatment intervals for EPN/MP and alternative cotton insecticides. The treatment intervals were developed cotton insecticides. The treatment intervals were developed in Mississippi (EPA, 1981j) and may not reflect pest management practices in other areas of the cotton belt where EPN is applied. If the synthetic pyrethroids are less persistent than indicated in Tables V-1 and V-2 the benefits of EPN will be larger.

C. Soybeans

The bulk of the nation's 71 million acres of soybeans are planted in the Corn Belt and in the southern half of the United States, except Texas. Within the South, soybean production is concentrated locally in the Mississippi Delta states of Arkansas, Louisiana, and Mississippi, where soybeans and cotton are the major components of commercial agriculture.

1. Use of EPN and Alternatives

EPN in combination with methyl parathion and/or toxaphene[20] is registered for the control of a variety of leaf and pod feeding soybean pests. As with cotton, the most widely used EPN product is the 3-3 emulsifiable concentrate formulated in combination with methyl parathion (EPN/MP). While recommended dosages range from 0.25 to 0.75 pounds of active ingredient per acre each of EPN and Methyl parathion, growers tend to apply this compound at or near the minimum recommended rate.

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[20] On November 29, 1982, the Agency published a notice of intent to cancel the use of toxaphene (FR 47 (229) :53784-53793. 1982). The cancellation of the insecticidal use of toxaphene on soybeans becomes effective at the end of the statutorily prescribed 30-day period.

The bulk of EPN use on soybeans occurs in the four south central states of Alabama, Arkansas, Louisiana, and Mississippi, where it is used primarily for control of the bollworm (Heliothis zea). Two likely (but not probable) hypotheses for the localization of EPN use have been identified:

1) Since EPN/MP is used in the control of various cotton pests in the South Central Region it is readily available for use on soybeans, and professional professional applicators are already familiar with and well trained in the application of EPN/MP.

2) EPN/MP is used in those areas where the bollworm has developed resistance to alternative insecticides.

Actual figures for EPN use on soybeans are not available. However, local extension experts have estimated the number of acre-treatments to range from 203,000 to 685,000 annually (Table V-3). Based on these estimates, EPN's market share in the region where it is most widely used would not exceed 20 percent of acre-treatments made annually (Table V-3). On a national level EPN's market share would not be expected to exceed 20 percent and would most likely be much smaller.

Table V-3. Estimated Annual Average Use of EPN and Major Alternatives on Soybeans in South Central Region, 1977-1980a/

Insecticide	Acre-Treatment (000's)	Percent of Acre-Treatments (%)
EPN/MP	203-685[c]	5.3 - 20.4
Carbaryl	118[d]	3.1 - 3.5
Methomyl	906[d]	23.6 - 27.0
Methyl Parathion	1233-751[d] [e]	32.1 - 22.4
Toxaphene/MP[b]	356[d]	9.3 - 10.6
Other	1026-544[d] [e]	26.7 - 16.2
TOTAL	3842-3360[d][e]	100

a/ As used here, the South Central Region includes the following states: AL, AR, KY, MS, and TN

b/ Notice of intent to cancel use of toxaphene published in Federal Register on November 29, 1982. FR 47(229): 53784-53793. 1982).

c/ Source: Based upon estimates from local experts; all EPN used in AL,AR, LA, and MS.

d/ Source; EPA estimates for 1977-1980.

e/ Range reflects uncertainty with regard to usage of EPN/MP.

2. Comparative Efficacy and Control Costs

A search of the literature revealed no data comparing the efficacy of EPN and alternatives for the control of soybean pests. In the absence of any evidence to the contrary, it was assumed for analytical purposes that both carbaryl and methomyl are as effective as EPN/MP for the control of bollworm (the key target pest of current EPN/MP use) on soybeans. Since bollworm resistance to methyl parathion has been reported (USDA-EPA-States, 1980), the latter has been excluded from consideration as a feasible alternative to EPN/MP for bollworm control.

From Table V-4, it can be seen that EPN/MP is the least costly insecticide when a comparison is made at the lowest application rates with the various alternatives. However, at the intermediate rates (i.e., at the mid-point of the range of recommended rates), carbaryl is less costly than EPN/MP.

Table V-4. Cost of EPN/MP and Alternatives at Various Application Rates

Insecticide	Application Rate (lbs. a.i. per acre)	Source of Recommended Rate a/	Cost of Insecticide Per Pound Active Ingredient e/f/ ($)	Cost of Insecticide Per Acre-Treatment ($)
EPN/MP b/			3.86 + 2.04	
low c/	.25 + .25	2		1.48
	.40 + .40	1		2.36
	.50 + .50	2 4		2.95
high d/	.75 + .75	1		4.43
carbaryl			2.15	
low	0.75	3 4		1.61
	1.00	1 2 3		2.15
high	1.50	1 2		3.23
acephate			6.99	
low	0.50	2		3.50
	0.75	1 2 3		5.24
high	1.00	1 4		6.99
methomyl			11.83	
low	0.25	2		2.96
	0.45	1 3		5.33
high	0.50	2 4		5.92
methyl parathion			2.20	
	1.0	1 2 3 4		2.20
tox/MP			0.76 + 2.15	
low	1.0 + 1.0	2		2.91
high	2.0 + 1.0	2		3.67

a/ Numbers identify sources as follows:

1. Alabama state recommendations, 1979.
2. Arkansas state recommendations, 1979.
3. Louisiana state recommendations, 1980.
4. Mississippi state recommendations, 1980.

b/ These are rates given in the state recommendations.

c/ This was the lowest rate that was recommended by any of the four states.

d/ This was the highest rate recommended by any of the four states.

e/ Sources: local soybean extension experts.

f/ Prices shown here are averages of the prices reported for a given chemical in the four states.

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3. Economic Impacts Due to Cancellation of EPN: User Impacts

Given that equal efficacy was assumed between EPN/MP and its alternatives, the only potential impact on soybean producers resulting from the cancellation of EPN would be an increase in treatment costs. Since methyl parathion has been ruled out as an alternative to EPN/MP due to efficacy considerations vis-a-vis the bollworm, only carbaryl, methomyl, and toxaphene/methyl parathion (tox/MP) were considered as alternatives for this analysis.[21] Because tox/MP is recommended only by the state of Arkansas, its use as an alternative to EPN/MP was assumed to occur only in that state.

In view of the foregoing assumptions, a weighted average change in cost per acre-treatment by state was calculated, the weights reflecting current usage shares among the equally efficacious alternatives to EPN/MP. The cost increase due to cancellation of EPN would range from a low of $1.39 per acre-treatment in Arkansas to a high of $2.60 per acre-treatment in Alabama. This variation reflects differences among states in recommended application rates.

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[21] A notice of intent to cancel the use of toxaphene was published in the Federal Register on November 29, 1982 (FR 47(299):53784-53793, 1982).

To determine the potential impact resulting from the simultaneous cancellation of EPN and toxaphene, a weighted average cost change was calculated, with methomyl and carbaryl considered as alternatives (Table V-5). As noted above, however, this eventually is relevant only for the state of Arkansas. Moreover, as calculated here (Table V-5), the cancellation of toxaphene would result in a (weighted average) cost savings of $0.02 per acre-treatment. This seeming anomaly occurs because, at the minimum recommended rates in Arkansas, tox/MP costs nearly as much as methomyl (the leading alternative to EPN/MP for bollworm control) and substantially more than carbaryl.

When the cost changes per acre-treatment (Table V-6) are multiplied by the estimated number of acre-treatments currently made with EPN/MP, the aggregate change in soybean insecticide costs is thus derived. As shown in Table V-6, the potential impact to soybean producers resulting from the cancellation of EPN would range from about $0.4 to $1.4 million annually.

D. Field Corn

Unlike many crops which are confined to certain regions of the United States due to agronomic and/or weather factors, field corn is grown throughout the nation. Of the eighty million acres planted annually, however, 61 million acres (76 percent) are found in the Corn Belt States: IL, IN, MI, MN, MO, NE, OH, SD, and WI.

Table V-5. Cost Per Acre-Treatment With/Without EPN/MP by State [a]

State	Cost Per Acre-Treatment With EPN/MP [b] ($)	Cost Per Acre-Treatment With Alternatives to EPN/MP--Toxaphene Available [c] ($)	Cost Per Acre-Treatment With Alternatives to EPN/MP--Toxaphene Not Available [d] ($)	Change in Cost Per Acre-Treatment Due to Cancellation of EPN Only ($)	Change in Cost Per Acre-Treatment Due to Cancellation of EPN and Toxaphene ($)
Alabama	2.36	4.96	4.96	+2.60	+2.60
Arkansas	1.48	2.89	2.87	+1.41	+1.39
Louisiana	2.95 [e]	4.90	4.90	+1.95	+1.95
Mississippi	2.95	5.42	5.42	+2.47	+2.47

[a] Table entries represent insecticide costs only.

[b] Based upon costs for minimum recommended application rates from Table 10.

[c] Weighted average of costs for minimum recommended application rates from Table 10. For AL, LA, and MS, the weights are as follows: carbaryl=0.115; methomyl=0.885. For AR, the weights are: carbaryl=0.086; methomyl=0.657; tox/MP=0.2580. The weights represent the hypothesized shares of acre-treatments potentially attained by the equally-efficacious alternatives to EPN/MP.

[d] Weighted average of costs for minimum application rates from Table V-8. The weights used here are the same as shown in Footnote "c" above.

[e] Although not recommended, EPN/MP is nevertheless used in Louisiana (USDA-States-EPA, 1980). It is assumed that growers apply EPN/MP at the same rate as in the neighboring state of Mississippi.

Table V-6. Estimated Changes in Treatment Costs Due to the Cancellation of EIN

State	High Estimate Change in Cost per Acre-Treatment a/ ($)	High Estimate Acre-Treatments Currently Made with EIN/MP b/	High Estimate Change in Aggregate Treatment Costs (000's)	Low Estimate Change in Cost per Acre-Treatment a/ ($)	Low Estimate Acre-Treatments Currently Made With EIN/MP c/	Low Estimate Change in Aggregate Treatment Costs (000's)
Alabama	2.60	10,000	26.0	2.60	2,963	7.7
Arkansas	1.41	250,000	352.5	1.41	74,088	104.5
Louisiana	1.95	50,000	97.5	1.95	14,818	28.9
Mississippi	2.47	375,000	926.3	2.47	111,131	274.5
Total	—	685,000	1,402.3	—	203,000 d/	415.6

a/ From Table V-5.
b/ From Chapter V of the EIN Benefit Analysis.
c/ State estimates derived by pro-rating according to the relative weights for the high estimate.
d/ From Table V-3.

1. Use of EPN and Alternatives

EPN is formulated as an emulsifiable concentrate, a granular product, and as a wettable powder for treatment of corn pests. The formulation and dosage actually used are primarily a function of the designated target pest. For treatment of the European corn borer, granular formulations at 0.5 pounds of active ingredient per acre are most commonly used. To control the silk-clipping activity of the corn rootworm adult beetle, producers use emulsifiable concentrates exclusively, at a dosage ranging from 0.19 pounds (when the EPN formulation is combined with methyl parathion) to 0.25 pounds of active ingredient per acre.

Since a substantial portion of corn acreage is treated preventively with a soil-incorporated insecticide for corn rootworm larvae control, the alternative insecticides used for this purpose have come to dominate the corn pesticide market. Because EPN is not registered for corn rootworm larvae control, most pesticide dealers prefer to stock rootworm larvicides which are also effective against European corn borer and other secondary pests (USDA-EPA-States, 1980).

The estimated use of EPN and selected alternatives in a normal year is shown in Table V-7. While carbofuran, terbufos, fonofos, and phorate constitute the leading corn insecticides for all pests taken together, a classification of insecticidal use according to target pest would produce a different ranking. Terbufos, a soil-incorporated insecticide, is not registered for European corn borer control; therefore, for analytical purposes it has not been considered as an alternative to EPN. Although not a leading insecticide for all corn pests as a whole, parathion is a leading alternative to EPN for the control of adult corn rotworm beetles.

2. Comparative Efficacy and Control Costs

On the basis of the limited test data available, it can be concluded that several alternatives to EPN are available for control of the European corn borer. No test-plot data were available regarding the relative efficacy of insecticides used for the control of corn rootworm adult beetles. In the absence of any information to the contrary from RPAR rebuttals and the literature, equal efficacy of EPN and its alternatives was assumed for analytical purposes.

Since EPN is used for control of both European corn borers and corn rootworm beetles, a comparison of costs between EPN and its alternatives must be target-pest specific (Table V-8 and Table V-9). For treatment of both target pests, there are alternatives both more costly and less costly than EPN.

Table V-7. Estimated use of EPN and Alternatives in a Normal Year, All Pests

Insecticide	Acre-Treatments (000s)	Percent of Acre-Treatments (%)	Dosage (lbs. a.i. acre)	Quantities a.i. applied (000s lbs.)
Carbofuran	12,716	33.2	1.00	12,716
Terbufos	7,146	18.6	1.50	10,719
Fonofos	6,802	17.7	1.00	6,802
Phorate	4,125	10.8	1.00	4,125
Parathion	574	1.5	0.25	93
EPN	164	0.4	0.50[b/]	82
Other	6,798	17.7	-	-
TOTAL	38,325	99.9[a/]	-	-

a/ Column does not add up to 100.0 due to rounding errors.

b/ Appropriate for granular formulation for European corn borer control.

SOURCES: EPA estimates; USDA-EPA-States (1980).

Table V-8. Per-Acre Treatment Cost for European Corn Borer: EPN vs. Alternatives

		Dosage (lbs. a.i./acre)			Cost Per lb. of a.i	Cost Per Acre-Treatment[a/]
Insecticide	Formulation	Low/Normal/High			($)	($/Acre)
Carbofuran	10%G	1.0	1.0	1.0	8.50	8.50
Fonofos	20%G	1.0	1.0	1.0	6.50	6.50
Phorate	15%G	1.0	1.0	1.0	5.13	5.13
EPN	4%G	0.2	0.5	0.5	14.25	7.13

[a/] Calculated at normal dosage; excludes aerial application cost of $3.50 per acre.

Source: USDA-EPA-States (1980).

Table V-9. Per-Acre Treatment Cost for Corn Rootworm Beetle: EPN vs. Alternatives

Insecticide	Formulation	Dosage (lbs. a.i./acre)	Cost Per lb. of a.i ($)	Cost Per Acre-Treatment[a] ($/Acre)
Carbaryl	80%S	1.0	3.14	3.14
	4 lb/gal EC w/oil	1.0	3.67	3.67
Parathion	4 lb/gal EC	0.25	2.50	0.63
Malathion	5 lb/gal EL	1.0	3.60	3.60
EPN/MP	3 lb/3 lb per gal EC	0.1875/ 0.1875	4.67	1.75
EPN	4 lb/gal EC	0.25	5.70	1.43

[a] Calculated at normal dosage; excludes aerial application cost of $3.50 per acre.

Source: USDA-EPA-States (1980).

3. Economic Impacts Due to cancellation of EPN

a. User Impacts

Based on the assumption that EPN is no more efficacious than any of its alternatives for controlling either European corn borer or corn rootworm adults, the cancellation of EPN would result in no yield changes; therefore, the only impact on EPN users would be a change in treatment costs for corn acreage formerly treated with EPN. In the absence of any empirical basis for predicting the alternatives which would actually be chosen, a weighted average has been used to calculate a composite per-unit change in treatment costs, the weights being the present market shares of the respective alternatives, Tables V-10.

When the composite (weighted average) change in cost per acre-treatment is multiplied by the number of acre-treatments normally made with EPN, the aggregate increase in production costs amount to about $30,000 per growing season (164,000 acre-treatments x $0.18 = $29,520). Given the imprecision of the underlying data, as well as the number of assumptions, it would be fatuous to insist upon the empirical relevance of this dollar impact. A reasonable interpretation of the foregoing result would be that the impact to producers resulting from the cancellation of EPN would range from none to negligible.

Table V-10. Composite Per-Acre Change in Treatment Costs Due to Cancellation of EPN

Selected Alternative Corn Insecticides (All Pests) [a]	Acre-Treatments in a Normal Year (000's)	Relative Share of Acre-Treatments (%)	Cost Per Acre-Treatment ($/Acre)	Change in Cost Per-Acre Treatment Due to Cancellation of EPN ($/Acre)
Carbofuran	12,716	52.5	8.50[c]	+ 1.37[c]
Fonofos	6,802	28.1	6.50[c]	- 0.63[c]
Phorate	4,125	17.0	5.13[c]	- 2.00[c]
Parathion	574	2.4	0.63[d]	- 0.80[e]
Total	24,217	100.0	---	+ 0.18[f]

a/ Although a leading corn insecticide, terbufos is used mainly for control of corn rootworm larvae, a pest for which EPN is not registered. Thus, terbufos is excluded from the list of EPN alternatives.

b/ From Table V-7.

c/ From Table V-8.

d/ From Table V-9.

e/ From Table V-9 calculated for price of EPN-4 E.C.

f/ Weighted average based on treatment shares of the respective insecticides.

b. Consumer Impacts

In view of the finding that the cancellation of EPN for the control of corn pests would have either no, or negligible, effects on producers, no impact on consumers is expected.

E. Pecans

U.S. pecan production is highly variable due to a combination of weather and agronomic characteristics peculiar to the pecan tree. In recent years, national production ranged from a low of 103.1 million pounds in 1976 to a high of 250.7 million pounds in 1978. Over the period 1974-1979, pecan production averaged 199.2 million pounds annually.

In 1978 Georgia was the largest producer of pecans followed by Texas, with 54 and 10 percent, respectively, of national production. The fact Texas and Georgia changed positions the following year, respectively accounting for 36 and 30 percent of the national crop, exemplifies the cyclical nature of pecan production.

1. Use of EPN and Alternatives

While EPN is registered for a variety of pests on pecans, it is commonly used for the control of the pecan weevil, the pecan nut casebearer, hickory shuckworm, aphids, and stinkbugs. Used for the control of these insects in only six states (AL, GA, OK, SC, TN, and TX), EPN accounts for only 3.4 percent of the total acre-treatments made annually for pecan insects. The leading alternative insecticides, each of which is more extensively used than EPN, are carbaryl, phosalone, and azinphos-methyl (Table V-11).

2. Comparative Efficacy and Control Costs

Based upon a review of the limited test-plot data found in the literature, it was concluded that there are alternative chemicals available which are as effective as EPN for the control of all of the major pecan pests. With regard to cost, there are several alternatives which are more costly and some which are less costly than EPN (Table V-12).

Table V-11. Estimated Use of EPN and Alternatives for Pecans in 1979 [a]/[b]

Insecticide	Acres Treated (000's)	Acre-Treatments (000's)[c]	Percent of Acre-Treatments (%) [d]	Dosage (lbs. a.i. per acre)[e]	Quantities of A.I. Applied [c] (000's of lbs.)
EPN	24.4	61.9	3.4	1.24	76.7
Carbaryl	205.4	732.6	40.5	2.57	1,882.3
Phosalone	133.7	329.3	18.3	1.01	331.8
Dialifor	80.1	289.8	16.0	1.58	458.0
Azinphos Methyl	186.3	385.2	21.3	0.94	362.7
Dimethoate	1.4	5.0	0.3	0.24	1.2
Disulfoton	1.4	5.0	0.3	0.66	3.3
Total	632.7	1,808.8	100.1	----	-----

[a] Includes usage only in states currently using EPN: AL, GA, OK, SC, TN, and TX.

[b] Estimates available for 1979 only ---- a year characterized by pecan extension entomologists as a "normal year" with respect to pest infestation levels.

[c] Where variables were stated as a range, the mid-point of that range was used to derive the estimates shown here. (EPA, 1981j).

[d] Column does not total to 100.0 due to rounding errors.

[e] Weighted average.

Sources: USDA - States - EPA, (1980); various local pecan extension experts

Table V-12. Cost Per Acre-Treatment: EPN vs. Alternatives

State b/	EPN 25 W	EPN 5 EC	Phosalone	Dialifor	Carbaryl 80S	Carbaryl 80W	Azinphos Methyl 2 EC	Azinphos Methyl 50 WP	Dimethoate	Disulfoton
	Chemicals a/									
	dollars									
AL	5.40	5.80	7.48	7.97	10.08					
GA	5.40	5.80	7.48 c/ 14.96	6.64 c/ 10.62	7.56					
OK	4.84		6.24	4.88		8.70				
SC		4.40	7.23	5.31	2.36 c/ 3.54		4.08		2.37	2.73
TN	d/	d/	7.23	5.31	7.08 c/ 14.16			6.11		
TX	4.84		6.42	4.88			6.27 c/ 9.41	6.00 c/ 9.00		

a/ Chemicals costs exclusive of application costs.

b/ Data presented only for states using EPN.

c/ Range in cost reflects underlying variation in application rates.

d/ No cost data for EPN available for Tennessee.

Sources: Various local pecan extension experts.

3. Economic Impacts Due to Cancellation of EPN

a. User Impacts

Given the assumption that the commonly used alternative insecticides are as effective as EPN in controlling pecan pests, the economic impact on growers resulting from cancellation can be measured by the change in treatment costs due to a shift to one or more alternative insecticides. The actual change in per-unit cost would vary substantially, depending upon the alternative chosen. In the absence of an empirical basis for predicting the post-cancellation market shares of the various alternatives, a weighted average was used to calculate a composite change in unit treatment costs, the weights being the present market shares of the respective alternatives. The resulting aggregate impact on growers would range from $3.26 to $11.79 per acre-treatment and from $164,000 to $173,000 in the aggregate (Table V-13).

b. Consumer Impacts

While the impact of EPN cancellation on a few growers may be substantial, depending upon individual circumstances and hence choice of alternative insecticides, the projected aggregate effect ($164 to $173 thousand) is negligible in terms of the total value of U.S. pecan production. According to the best estimates available, about 24,000 acres of pecans are treated with EPN, which account for about 4 percent of all pecan acres treated, and only 2 percent of the total pecan acreage in production.

Table V-13 Aggregate Impact on Pecan Growers Due to EPN Cancellation

State	Acres Currently Treated with EPN	Composite Change in Per-Acre Treatment Costs Low[b/]	Composite Change in Per-Acre Treatment Costs High[b/]	Aggregate Impact on Pecan Growers[a/] Low	Aggregate Impact on Pecan Growers[a/] High
		—— $/acre	——	—— 000's	——
AL	1,000	9.31	11.48	10.24	12.63
GA	1,500	5.90	9.83	8.85	14.75
OK	6,300	11.79	11.79	74.28	74.28
SC	500	3.26	3.47	1.58	1.74
TN	8	5.92	11.84	0.47	0.94
TX	15,000	4.58	4.58	68.70	68.70
Total U.S.	24,408 [c/]	-----	-----	164.12	173.04

[a/] Derivation: [Acres currently treated with EPN] x [composite change in per-acre treatment costs].

[b/] Derived from data in Table V-12. These figures reflect multiple treatments within the production season.

[c/] From Table V-11.

Assuming, for purposes of this document, that all acreage presently treated with EPN would be forced out of production due to increased treatment costs, and further assuming an average yield of 200 pounds of nuts per acre, annual production would fall by 4.9 million pounds, for a decrease of about 2.5 percent [4,881,600 pounds/199,233,000 pounds = .025] (EPA, 1981j). When it is considered that the average annual (absolute) deviation from the mean level of production is 52,756,000 pounds or 26.5% [52,756,000 pounds/199,233,000 pounds] for the period 1974-1979 (EPA, 1981j), the hypothesized decrease in production induced by the cancellation of EPN becomes very slight.

One cannot say with certainty that the cancellation of EPN would have no effect on pecan prices. On the other hand, given the relatively small acreage involved, and the extreme variability in quantities and prices due largely to weather factors, the price effect induced by the cancellation of EPN would be impossible to measure. Moreover, since equally efficacious alternatives are available at only slightly higher costs, it is highly unlikely that all or even a major portion of the acreage treated with EPN would be withdrawn from production following cancellation. In view of the foregoing considerations, the consumer impact due to the cancellation of EPN would be negligible.

F. Peaches

Accounting for 62 percent of the national crop in 1979, California is by far the leading state in peach production. South Carolina ranks as the second largest producer, with 12 percent of U.S. production in 1979 followed by Georgia (4.8 percent), Pennsylvania and New Jersey (3.1 percent each), and North Carolina (1.8 percent).

Reportedly, EPN is used as a peach insecticide only in the state of Georgia. Peach production there is concentrated in the central part of the state in an area comprised of Peach, Taylor, Crawford, Macon, and Houston counties. Present acreage is estimated at 21,300, managed by slightly fewer than 100 growers. The average size of a farm unit is about 220 acres, with 45 percent of the acreage on enterprises with 1,000 or more acres of peaches (EPA, 1981j)[22]

1. Use of EPN and Alternatives

Georgia was the only state in which EPN was used on peaches in 1979 and 1980 (USDA-EPA-States, 1980). EPN-Sulfur 1 1/2 Peach Spray 6 and EPN 25 W are used to control cat-facing insects (tarnished plant bugs, stink bugs, and leaffooted bugs) on peaches. These products are applied twice per season (once at petal-fall and once at shuck-fall) at the rate of 0.56 pounds of active ingredient. As shown in Table V-14, EPN accounts for less than 10 percent of total acre-treatments.

22/ Data on Georgia peach production was derived from preliminary results of a 1980 University of Georgia survey.

Table V-14 Estimated Use of EPN and Alternatives for Peaches in Georgia in 1979[a]

Insecticide	Acres Treated (000's)	Acre-Treatments (000's)	Percent of Acre-Treatments (%)[b]	Dosage (lbs. a.i. per acre)	Quantities of A.I. Applied (000's of lbs.)
EPN	1.8	3.5	8.0	0.5625	2.0
Phosmet	5.3	10.7	24.4	1.1250	12.4
Penncap-M®	5.3	10.7	24.4	0.7500	12.0
Parathion	6.4	12.8	29.2	0.4500	5.8
Azinphos Methyl	2.0	4.1	9.3	0.3750	1.5
Endosulfan	1.1	2.1	4.8	0.7500	1.6
Total	21.9	43.9	100.8	——	—

[a] Estimates for usage in a normal year not available.

[b] Column does not total to 100.0 due to rounding errors.

Source: EPA (1981j)

2. Comparative Efficacy and Control Costs

Based upon limited test data, it appears that the alternatives to EPN are equally efficacious for the control of cat-facing insects. In one test, parathion and EPN afforded equal control of these pests, while in several more recent tests several alternatives performed as well as parathion and hence, indirectly, as well as EPN (EPA, 1981j).

The unit cost of controlling cat-facing insects in Georgia with EPN and alternative is shown in Table V-15. At the application rates recommended by the local extension service, an acre-treatment with phosmet, parathion, or azinphos methyl is less costly than one with EPN. Both endosulfan and Penncap M® are more costly than EPN.

3. Economic Impacts Due to Cancellation of EPN

a. User Impacts

Given the assumption of equal efficacy among the commonly used alternatives to EPN, the only impact from cancellation of the latter would be a change in insecticidal treatment costs. In the absence of any information that would permit a prediction of the change in market shares following EPN cancellation, a composite (weighted average) change in per-unit treatment cost was calculated, with the present market shares of the respective alternatives serving as weights.

Table V-15. Cost per Acre-Treatment for Control of Peach Insects in Georgia: EPN vs. Alternatives a/

Product	Recommended Rate (lbs. a.i./acre)	Cost per Acre-Treatment ($)
EPN-Sulfur Peach Spray (5% EPN)	0.56	4.05
Phosmet (50W)	0.45	2.16
Parathion (15W)	0.45	1.98
Azinphos Methyl (50W)	0.37	3.75
Penncap M® (2E)	0.75	5.06
Endosulfan (50W)	0.75	6.75

a/ Exclusive of application cost.

Source: EPA (1981j)

The composite change is estimated at a reduction of $1.55 per acre, with the range of cost changes varying from - $4.14 to + $5.40 per acre, depending upon the alternative actually chosen.[23] It is interesting to note that the growers presently using EPN could reduce their treatment costs by $0.60 to $4.14 per acre if either azinphos-methyl, phosmet, or parathion were selected. Assuming equal efficacy among EPN and its alternatives, and also assuming that peach producers are economically rational, then other unknown factors must account for this behavior.

Aggregate impacts were calculated from a composite cost change (i.e., weighted average) multiplied by the affected acreage. From this calculation, is anticipated that cancellation would reduce treatment costs of producers currently using EPN from $1,779 to 3,669 annually. A commonsense interpretation of these anomalous results is that the cancellation of EPN would have no economic consequences for Georgia peach growers.

b. Consumer Impacts

Since the cancellation of EPN would entail no increase in production costs nor a decrease in yield, the price of peaches would be unaffected on either the local or national level. Therefore, no impact on the consumer is expected.

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[23] Values are derived from data in Table V-14 and Table V-15. Assumes two treatment per season.

G. Sweet Corn

Sweet corn has become one of the most important vegetable crops in terms of acreage and value. It is grown for processing in about 25 states, and for local markets and in home gardens throughout the country.

Between 1978 and 1980, an average of about 623 thousand acres of sweet corn were grown throughout the United States. About 71 percent (441,487 acres) of the acreage was for the process market, where the average market value received at the grower level was about $120.7 million per year. Wisconsin and Minnesota account for over half of the sweet corn acreage for the process market, while Florida and New York account for slightly less than half the acreage for the fresh market.

About 306,467 acres of sweet corn are grown in the North Central States (includes the following: IA, IL, MI, MN, and WI), and 99,332 acres are grown in the Northeast (includes the following: New England, NY, PA, NJ, MD, and DE). The average size of the sweet corn enterprise in these regions is about 43 acres.

1. Use of EPN and Alternatives

Although registered for a variety of sweet corn pests, EPN is used primarily for control of first and second generation European corn borer. Growers typically make

1 to 2 applications per season. Virtually all EPN usage occurs in the North Central and Northeast regions.

The extent to which EPN is used on sweet corn is not known with any degree of certainty. According to two recent estimates, annual use for control of European corn borer may be for as few as 22,000 acre-treatments or as many as 124,000 acre-treatments (USDA-EPA-States, 1980). Depending upon which estimate is most accurate, EPN accounts for anywhere from 4 to 20 percent of total acre-treatments made annually for European corn borer. The major alternatives used are methomyl, carbaryl, parathion, parathion + carbaryl, and Penncap M® (Table V-16).

2. Comparative Efficacy and Cost

There is little information available concerning the comparative effectiveness of EPN and alternative insecticides used on sweet corn. In trials conducted in New York, EPN was found to be equal or superior to methomyl and encapsulated methyl parathion (Penncap M®) for the control of the European corn borer. Further field trails are needed to provide data necessary for a rigorous assessment of the relative efficacy of EPN and alternatives. In view of the limited data available, and in absence of any information to the contrary, it was assumed that the major alternative insecticides are at least equally as effective as EPN for control of European corn borer. Of the alternative chemicals available, some are more costly and some are less costly than EPN (Table V-17).

Table V-16. Estimated Use of EPN and Alternatives for Sweet Corn for European Corn Borer in the North Central and Northeast Regions in a Normal Year

Insecticide	Acre-Treatments (000's)[a]	Percent of Acre-Treatments (%)	Dosage (lbs. a.i./acre)	Quantities of A.I. Applied (000's lbs. a.i.)
EPN	12-124[b]	4-20	0.36	7.9-44.6
Methomyl	168	32-27	0.36	60.5
Carbaryl	159	31-26	1.50	238.5
Parathion	99	19-16	0.75	74.3
Penncap-M®	45	9-7	0.75	33.8
Other	28	5-4	----	----
Total	521-623	100-100	----	----

a/ Source: EPA estimates, 1980, except where otherwise noted.
b/ Source: USDA-EPA-States (1980)

Table V-17

Per-Unit Treatment Cost for European Corn Borer: EPN vs. Major Alternatives

Insecticide	Formulation	Dosage [a/] (lbs. a.i./acre)	Cost per lb. of a.i. ($)	Cost per Acre-Treatment [a/] [b/] ($/acre)
Methomyl	1.8 E	0.36	13.16	4.74
Carbaryl	80% S	1.50	3.15	4.73
Carbaryl/ Parathion	80% S, 8 EC	1.50/ 0.38	3.15/ 3.14	5.92
Parathion	8 EC	0.75	3.14	2.36
Penncap M®	Capsules	0.75	7.37	5.53
EPN	4% G	0.35[c/]	14.25	4.99
EPN	4 EC	0.38[c/]	5.88	2.23

[a/] Except where otherwise noted, estimates are based on the midpoint of the dosage ranges given in state recommendations of major sweet corn producing states.

[b/] Exclusive of application costs.

[c/] Estimate based on midpoint of dosage ranges found on the label.

Sources: USDA-EPA-States (1980); EPA (1981j).

3. Economic Impacts Due to Cancellation of EPN

a. User Impacts.

On the assumption that the available alternative insecticides are equally as efficacious as EPN, the only economic impact on growers resulting from the cancellation of EPN would be a change in insecticidal treatment costs.

For the impacted growers in the North Central Region (where EPN is primarily used in the granular formulation), use of alternative insecticides would result in a cost change ranging from a decrease of $2.63 per acre-treatment to an increase of $0.93 per acre-treatment. By contrast, in the Northeast (where EPN is primarily used as an emulsifiable concentrate), use of alternative insecticides would result in a cost increase ranging from $0.40 to $3.69 per acre-treatment.[24/]

The aggregate change in production costs for each region was estimated by multiplying the (respective) weighted average change in cost by the number of acre-treatments normally made with EPN.

[24/] A discussion of the differences in terms of formulation used between the two regions is found in Chapter VII of the "EPN Benefit Analysis" (EPA, 1981j).

Since there are no regionally disaggregated estimates of EPN usage available, it was assumed that the relative proportion of acres treated was equal to the proportion of sweet corn acreage grown in each region. Thus the North Central Region, which grows about 75.5 percent of the sweet corn acreage in the two regions, was assumed to have 75.5 percent (9,060-52,095 acres) of the EPN treated acreage. The Northeast Region, with 24.5 percent of the sweet corn acreage in the two regions, was assumed to have 24.5 percent (2,940-16,905 acres) of the EPN-treated acreage.

Based on the above assumptions, the aggregate change in costs for growers in the North Central region would be a decrease of $3,588 to $20,630 per year. By contrast, for the growers in the Northeast, production_costs would increase by $13,600 to $78,202 per year. The net change in cost for the two regions combined would be an increase of $10,012 to $57,573 per year (Table V-18).

Although these estimates are based on imprecise data and a number of assumptions, it is nevertheless safe to conclude that the cancellation of EPN would have a relatively small economic impact on the affected growers.

Table V-18. Aggregate Change in Treatment Costs Resulting from Cancellation of EPN Use on Sweet Corn

Region	Affected Acreage	Number of Acre-Treatments a/	Weighted Average Change in Cost per Acre-Treatment ($)	Aggregate Cost Change ($)
North Central	9,060 - 52,095 b/	16,308 - 93,771	- 0.22	- 3,588 to - 20,630
Northeast	2,940 - 16,905 c/	5,292 - 30,429	+ 2.57	+ 13,600 to + 78,203
Total	12,000 - 69,000	21,600 - 124,200		+ 10,012 to + 57,573

a/ Assumes 1.76 applications per season.
b/ Affected acreage in the North Central Region is assumed to be 75.5% of the total EPN treated acreage.
c/ Affected acreage in the Northeast Region is assumed to be 24.5% of the total EPN treated acreage.

b. Consumer Impacts

In view of the availability of effective alternative insecticides, the cancellation of EPN is expected to have little or no impact on the supply of sweet corn. Since only a relatively small percentage (2-11%) of the overall sweet corn acreage is treated with EPN, it is also reasonable to expect that the increased costs of alternative pesticides would be absorbed at the grower level, rather than passed on to consumers in the form of higher retail prices.

H. Miscellaneous Vegetables

1. Use of EPN and Alternatives

While EPN is registered for a variety of vegetable sites, only three such uses were analyzed by the designated EPN Assessment Team biologist (USDA-EPA-States, 1980). Of the crops thus analyzed (lettuce, tomatoes, and beans) apparently none has been treated with more than negligible quantities of EPN in recent years. It should be noted that the EPN Biological Assessment Team was unable to find any confirmed use of EPN for these crops outside of California. Within that state, moreover, EPN use has been extremely limited over the past several years--from nil in most years on lettuce to negligible quantities on tomatoes and beans (Table V-19). Since EPN is registered for lettuce in the State of California, it can be stated that the national use of EPN is also virtually nil.

Table V-19. Usage of EPN in California on Lettuce, Tomatoes, and Beans, 1972-1979

Years	Crops					
	Lettuce		Tomatoes		Beans	
	lbs. a.i.	acres	lbs. a.i.	acres	lbs. a.i.	acres
1979	—	—	203.4	260	—	—
1978	—	—	55.0	71	866.8	1460
1977	111.6	150	225.9	311	2546.3	3954
1976	—	—	62.0	50	1320.6	1771
1975	—	—	210.0	230	1812.5	2127
1974	—	—	—	—	4561.2	6152
1973	—	—	16.6	285	4742.8	7121
1972	--	—	1842.9	2264	5323.1	5922

Source: California State Department of Food and Agriculture, 1972-1979.

There are (at least) three factors which partially account for the limited use of EPN on these crops. First, with the exception of Ohio which recommends EPN for the control of mites on tomatos, EPN is not recommended by the states. Second, the requirement for a 21-day preharvest treatment interval severely diminishes the utility of EPN for the treatment of snapbeans. Finally, and perhaps most important, there are several available alternatives which are equally as, or more, effective than EPN.

According to the findings of an informal survey conducted for the Biological Assessment Team, one such widely used alternative on lettuce, tomatoes, and beans is dimethoate. Significantly, the Dimethoate RPAR Assessment Team did not consider EPN to be of sufficient importance to be cited as an alternative to dimethoate for the treatment of these crops.

Reflecting this pattern of limited usage is the lack of interest of the basic manufacturers in retaining EPN labels for vegetable crops. To wit:

1) The DuPont Company has requested the revocation of tolerances for several crops, including lettuce, tomatoes, and beans, which constitute minor uses of EPN.

2) In its rebuttal to EPA, the Marubeni America Corporation discussed only cotton, soybeans, and pecans.

3) Similarly, the rebuttal submitted by the Velsicol Corporation discussed only cotton, corn (field and sweet), and soybeans.

2. Economic Impact Analysis

a. Present Benefits of EPN

In view of the fact that only negligible quantities of EPN are used on lettuce, tomatoes, and beans, the present benefits from such use are zero. That such is the case has been explicitly recognized by the Velsicol Corporation in its RPAR rebuttal wherein it is noted that the continued registration of EPN on beans (among other sites) "...must be defended on potential uses rather than current use."

b. Potential Benefits of EPN

The case of potential benefits rests on two arguments, neither of which can be definitively affirmed or negated:

1) Availability. According to Velsicol, EPN could have been sold for use on beans in the Delmarva Peninsula in 1979 had the product been available.

2) Resistance. It has been stated that the availability of a suitable alternative chemical (in this instance EPN) is needed should resistance to the preferred pesticide develop (USDA-EPA-States, 1980).

Given that both of the foregoing arguments are highly conjectural, no attempt has been made to quantify any such potential benefits.

I. Control of Mosquitoes in Aquatic Areas

According to the findings of the Biological Assessment Team, there is no use of EPN in current mosquito control programs (USDA-EPA-states. 1980). While extremely small quantities of EPN have in fact been used in California in the past, there is currently no use of EPN in the mosquito abatement programs, in that state.[25]

Given that EPN is currently used to only a negligible extent for mosquito control, the present benefits are negligible.

J. Summary of Aggregate Use and Economic Impacts Due to Cancellation of EPN

Overall annual impacts due to the cancellation of EPN are summarized in Table V-20. Individual growers on some sites would sustain a modest increase in insecticidal treatment costs; and in isolated cases more substantial benefits from EPN use may occur due to specific environmental conditions (pest spectrum, weather, etc) however, the aggregate impact ranges from negligible to minor, depending on the particular site.

Economic impacts at the processor and consumer levels are not anticipated from an EPN cancellation.

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[25] California's use of EPN for mosquito control amounted to an annual average of 69 pounds of active ingredient in the period 1974-1979.

Table V-20

Aggregate Use and Economic Impacts Due to Cancellation of EPN

Site/Scenario	Extent of Use				Annual Impacts Due to Cancellation of EPN or EPN and Toxaphene			
	Acre-Treatments (000's)	Percent of Acre-Treatments (%)	lbs. of A.I. (000's)	Percent of lbs. of A.I. (%)	Availability of Economic Alternatives	Nature	Significance	Economic Impacts ($000) a/
Cotton					Several, but set of alternatives varies according to target pest.	Negligible impacts, generally less expensive alternatives available.	In isolated cases, growers may experience benefits of $2.00 per acre. Negligible significance in aggregate at user, processor, or consumer level.	
Low Estimate	2,500	84.7	1,500	85.8				0
High Estimate	4,500	82.4	2,700	84.7				175 b/
Field Corn					Several, but set of alternatives varies according to target pest.	Increased treatment costs for growers currently using EPN.	Slight for current EPN users; negligible for processors and/or consumers.	
Low Estimate	164	5.6	82 c/	4.7				30
High Estimate	164	3.0	82	2.6				30
Soybeans					At least two, perhaps more, depending upon target pest.	Increased treatment costs for growers in AL, AR, LA, and MS.	Minor for current users of EPN; negligible for processors and/or consumers.	
Low Estimate	203	6.9	83	4.7				400
High Estimate	605	12.4	279	8.8				1,400
Peaches								
Low Estimate	2	<0.1	1	<0.1	Several	No change in treatment cost.	-	-
High Estimate	5	<0.1	3	<0.1				
Pecans								
Low Estimate	62	2.1	74	4.2	Several	Increased or decreased treatment costs for growers in AL, GA, OK, SC, TN, and TX, depending upon which alternative is selected.	Minor	164
High Estimate	66	1.2	79	2.5				173
Sweet Corn								
Low Estimate	22	0.7	8	0.5	Several	Increased treatment costs to growers in Northeast Region.	Minor for current users of EPN, negligible for processors and/or consumers.	10
High Estimate	124	2.2	45	1.4				58
Misc. Vegetables	Negligible	-	Negligible	-	Several	-	-	Negligible
Mosquito Control Aquatic Areas	Negligible	-	Negligible	-	Several	-	-	Negligible
Total								
Low	2,953	100.0 d/	1,748	100.0 d/	-	-	-	604
High	5,464	100.0 d/	3,188	100.0 d/	-	-	-	1,836

a/ Economic impacts reported in 1980 dollars for all crops except cotton which is reported in 1982 dollars.
b/ Estimates assume per acre benefits on 3.5 million acre-treatments.
c/ Assumes that all acreage is treated at a rate appropriate for European corn borer (0.5 lbs. a.i. per acre).
d/ Columns may not total precisely to 100.0 due to rounding errors.

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VI. IDENTIFICATION AND SELECTION OF REGULATORY ACTIONS

A. Introduction

Chapters III, IV and V examined the human and environmental risks associated with the uses of EPN, and identified the benefits associated with each major use. As described in Chapter I, FIFRA mandates that the Agency weigh the human and environmental risk against any economic benefits of the use(s) of a pesticide in order to determine whether uses can continue without unreasonable adverse effects. To carry out that mandate, there is a wide range of regulatory options available to the Agency. For each use pattern, the Agency evaluates each feasible regulatory option for its impact on both sides of the risk/benefit equation, and then selects the most appropriate course of regulatory action.

This Chapter describes the process by which the Agency developed potential regulatory options for EPN, provides a risk/benefit analysis for each of the options, and sets forth the regulatory measures which the Agency has decided are most appropriate to adopt and implement.

B. Legal Basis for Options

FIFRA provides the Administrator with three broad legal courses of action for a pesticide which is the subject of a rebuttable presumption against registration. These are:

1) continue registration without additional restriction;

2) continue registration, but amend the terms and conditions of registration; and

3) cancel registration.

Continued registration without restriction (Option 1) and cancellation (Option 3) are options which correspond to the opposite ends of the risk/benefit spectrum. Briefly, cancellation means that the sale and distribution of the pesticide at issue is prohibited; continued unrestricted registration means that sale and distribution are continued unchanged. Adoption of Option 1 is appropriate when the Agency concludes that the level of risk is reasonable in light of the pesticide's benefits and that further risk reduction measures are not necessary to assure that the use of the pesticide meets the statutory standard for continued registration.

Adoption of Option 3, cancellation, is appropriate when the Agency concludes that the risks from a use or uses outweigh the benefits of the use(s) and that these risks cannot be mitigated to a reasonable level, in light of the benefits, by any other measures short of cancellation. The effect of cancellation is to eliminate entirely both the risks of a pesticide's use or uses and the benefits of the use(s). Cancellation may affect all uses of a compound, or it may affect only specific uses, or specific formulations, or specific application methods. Cancellation may be conditioned on the completion of studies, or it may be delayed for a specified period of time to allow for development and implementation of satisfactory alternative pest control measures. Finally, the terms of cancellation may provide for the continued sale and use of existing stocks of the cancelled pesticide to such extent, under such conditions, and for such uses as would be consistent with FIFRA.

In the case of cancellation, the Administrator issues a notice of intent to cancel any or all registrations of pesticide products which are registered for the specified use(s) [FIFRA Section 6(b)(1).[26] Unless otherwise specified, such a cancellation notice becomes effective 30 days after receipt by the registrant or publication of the notice in the Federal Register, unless 1) the registration(s) are modified to the Agency's satisfaction or 2) a registrant or other adversely affected person requests a hearing on the cancellation of one or more registrations.

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[26] Cancellations may also be the result of FIFRA section 6(b)(2) hearings. Because a 6(b)(2) hearing is not being proposed for EPN, it is not discussed in this document.

Between these polar alternatives of continued registration without restriction and cancellation exists a range of possible regulatory actions. In fact, FIFRA requires that the Administrator shall "consider restricting a pesticide's use or uses as an alternative to cancellation..." [FIFRA Section 6 (b)]. Although FIFRA does not specify what kinds of restrictions are to be examined, the Agency interprets this to mean amending the terms and conditions of registration in any fashion appropriate for the uses in question.

Adoption of this option is appropriate when the risks of a pesticide use can be reduced to a reasonable level, while preserving the benefits of the use, by modifying the terms and conditions of the pesticide's registration. These modifications, which are generally expressed through the pesticide's labeling, often include changes in the way the pesticide is used, the purposes for which it may be used, or where it may be used. Such changes in use are usually designed to reduce exposure of humans or animals to the pesticide, and thereby to reduce or even eliminate the risk from the pesticide.

C. Development of Regulatory Options

The development of regulatory options short of cancellation involves the formulation of modifications to the terms and conditions of registration which are intended to reduce the risks attendant to the use(s) of the pesticide. Each option is then evaluated to determine whether it achieves an adequate reduction in risk without causing unreasonable economic consequences, such that the remaining benefits of the use exceed the remaining risks of that use.

The risks which the Agency considered to be attendant to the uses of EPN were: 1) delayed neurotoxicity; 2) reductions in local/regional populations of nontarget organisms (honeybees); and 3) acute toxicity to aquatic organisms resulting from the use of EPN as a mosquito larvicide.

The risks of delayed neurtoxicity to humans from EPN residues on food and from applicator exposure have been quantitatively analyzed and the Agency has determined, based on a range of NOEL's, that an ample margin of safety exists for the general population (dietary exposure), and for the following applicator groups: airplane pilots, mixer/loaders, and ground applicators. An ample margin of safety does not exist for flaggers, however. See Chapter IV, Section C on Human Risk Assessment, for a discussion of the margins of safety.

Therefore, the process of developing a full range of regulatory options, with respect to pesticide products containing EPN, focused on ways to 1) reduce levels of exposure to EPN applicators, 2) protect bystanders who might be exposed to EPN as a result of wind drift, 3) alleviate exposure and risk to honeybees, and 4) minimize exposure and risk to aquatic organisms (mosquito larvicide use). By definition, such exposure reduction measures would result in comparable reductions in risk.

The Agency has assessed the various exposure situations at issue and has examined a number of specific measures by which exposure and risk might be reduced via amendments to the terms and conditions of registration. The risk reduction measures discussed in the following subsections have been assessed, taking into account potential effectiveness as well as economic and practical feasibility.

1. Restrictions Aimed at Reducing Occupational Risks of EPN

The Agency examined the following measures designed primarily to reduce the risk of EPN exposure to applicators and other handlers of the pesticide.

a. Classify EPN for Restricted Use Only and Require Applicator Certification

Under FIFRA, pesticides may be classified for restricted use and limited to use only by certified applicators. On August 1, 1979 the Agency published a proposed rule in the Federal Register which would amend 40 CFR 162.31 by adding uses of active ingredients to be classified for restricted use under 40 CFR 162.30.[27/]

On January 19, 1981, the Agency published a final rule in the Federal Register to add certain uses of eight active ingredients (including EPN) to the list of uses which the Agency has classified for restricted use (46 FR 5696). The final rule regarding EPN classification became effective on June 10, 1981 [46 FR 29708], whereas all uses of EPN liquid and dry formulations (granular and wettable powder) greater than 4% were classified for restricted use. This reclassification occurred subsequent to the publication of PD 1, independent of the RPAR process, and resulted in most end-use formulations of EPN being classified for restricted use. Granular EPN formulations with 2% or less active ingredient (a.i.), however,remain classified for general use. Pursuant to an Agency policy decision, the classification of low percent EPN granular formulations is to be considered together with other low a.i. granular formulations. This decision will not be specific to EPN and lies outside the scope of this RPAR review.

[27/] This proposed rule was based on the risk criteria for determining a pesticide's use classification, as provided in 40 CFR 162.11 (c)(2) through (5), which require that determinations concerning the use classification of a pesticide must take into account the pesticide's existing toxicity category, the level of risk posed to humans and the environment, the adequacy of present labeling, and other hazard information. Under the proposed rule all EPN liquid and dry formulations greater than 4% and all EPN granular formulations 2% and greater would be classified for restricted use (44 FR 45218).

b. Standardize Label Requirements for Protective Clothing, Goggles, and Respirators; Require Labels to Feature the Phrase PROTECTIVE CLOTHING REQUIRED Prominently in Bold Face Type

Current EPN labels generally direct that persons involved in application procedures wear protective clothing, goggles, and a respirator, though some labels cite either a mask or a respirator, and labels are not consistent as to whether or which particular items of protective clothing are specified.

In addition, the current label format is such that directions concerning protective clothing are generally not featured in a prominently fashion.

As a means to ensure that dermal and respiratory exposure is minimized, the Agency has explored the standardization of EPN label directions to specify particular articles of protective clothing, and to require that the phase protective clothing appear prominently in bold face type.

Pilots of airplanes and helicopters are exempt from this protective clothing requirement when flying aircraft, although the Agency would encourage the use of aircraft equipped with positive ventilation equipment. Pilots involved in the mixing-loading operation would be required to wear protective clothing and equipment during that operation.

Table IV-10 lists the estimated exposure to applicators when no protective clothing or respirators are worn. This was the exposure estimate used by the Agency in PD-1. However, the Agency in this document has proceeded on the revised assumption that protective clothing and a respirator are worn as current labels direct. Table IV-12 reflects the estimated exposure when protective clothing and a respirator are worn. It should be noted, however, that while the Agency has proceeded on the assumption that current label directions for protective clothing are generally followed and that the protective clothing and respirators are in good repair and worn at all times that an exposure potential exists [28] the Agency remains concerned about any possibility of miscompliance.[29]

Recently, completely closed systems have been developed for the mixing, loading and application of pesticides. Ideally, proper use of an appropriate, working, closed system should eliminate all exposure since applicators rarely come into direct contact with the pesticide during closed system applications. It is estimated that exposure (dermal and respiratory) for most applicators could potentially be reduced to insignificant levels through the use of these systems. Accordingly, requirements for protective clothing and respirators could be waived for most applicators when a closed system of application is used. However, because their activities are unaffected by the use of closed systems application, flagger exposure and the need for protective measures would remain the same as with the more conventional application methods.

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[28] The latter consideration is particularly important because of the extremely hot weather conditions found in the areas (primarily the Southeast) where cotton and soybeans are treated with EPN.

[29] Allegations of miscompliance were cited in PD 1, and the results of a recent survey conducted by the National Agricultural Aviation Association (NAAA) suggest that in isolated instances growers functioning as flaggers might be working without protective clothing and without the protection of an enclosed vehicle. [See Section VI.B.2.c of this document.]

In the Agency's judgement, label directions which are standardized and featured prominently on the label would help to ensure that unnecessary dermal and respiratory exposure during application procedures does not occur. The economic impacts of these and other label modifications considered below are projected as negligible.

c. Prohibit Human Flaggers Unless Protected by a Totally Enclosed Vehicle

As determined by the Agency's exposure and risk analysis, human flaggers are the applicator group which is subject to the greatest exposure potential. This potential is significant even when adjustments for protective clothing and respirators are included in the exposure assessment.[30]

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[30] Even when protective clothing and respirators are worn there is not an ample margin of safety for this group of applicators.

Flaggers are individuals stationed at predetermined points in a field who indicate to pilots applying EPN where to begin (or stop) applying the pesticide. As a result, these individuals can come into direct contact with the pesticide and are at substantial risk as indicated in Table IV-12. This registration modification could eliminate this unreasonable risk by requiring use of automatic flagging devices or fully protective enclosures for flaggers.

Based on the limited information available, it is not possible to quantify the economic impacts likely to result if human flaggers are prohibited unless they work from fully protective enclosures. Recognizing that human flaggers might be deemed necessary (or desirable) by small cotton producers whose fields are situated in hilly and wooded areas, the Agency nonetheless projects that such impacts would be limited.

2. Measures Considered as Means to Prevent Exposure to Bystanders

In the event of application during weather conditions favoring wind drift, unprotected bystanders could be subject to exposure to EPN. Recognizing that current labels generally direct users not to apply EPN during wind drift conditions, the Agency has considered proposing that a standard label warning be required which specifies that EPN must not be applied during weather conditions favoring wind drift.

3. Measures Considered as Means to Protect Honeybees from Exposure and Risk

This registration modification would protect honeybees from exposure to EPN. The Agency believes that label warnings which are specific to crops would more effectively achieve the desired result.

a) For all wettable powder (WP) and emulsifiable concentrate (EC) formulations of EPN [to appear in the "Environmental Hazards" section of the label]: "This product is highly toxic to bees exposed to direct treatment or residues on blooming crops or weeds. Do not apply this product or allow it to drift to blooming crops or weeds if bees are visiting the treatment area.

b) For WP and EC formulations of EPN labeled for use on stone fruits, pome fruits and citrus [to appear in the "Use Directions" section of the label]: "Do not apply when trees or a substantial number of weeds in the orchard/grove are in bloom."

c) For WP and EC formulations of EPN labeled for use on field and/or sweet corn [to appear in the "Use Directions" section of the label]: " Do not apply to corn during the pollen-shed period if bees are visiting the treatment area."

d) For WP and EC formulations of EPN labeled for use on cotton [to appear in the "Use Directions" section of the label]: "Do not apply to blooming cotton if bees are visiting the treatment area."

4. Measures Considered as Means to Reduce Exposure and Risk to Aquatic Organisms (Mosquito Larvicide Use Only)

To protect aquatic species from exposure and risk as a result of EPN use as a mosquito larvicide, the Agency has considered amendments to the terms and conditions of registration:

a) Prohibit aerial applications.

b) Limit applications to stagnant or otherwise non-fish bearing waters.

c) Allow use only to prevent a human health hazard.

Because EPN is reported rarely used as a mosquito larvicide, impacts are not expected in connection with any of the above measures.

D. Selection of Regulatory Options

As noted earlier, the Agency considers EPN to pose the following risks to humans and the environment: 1) delayed neurotoxicity; 2) reductions in local/regional populations of nontarget organisms (honeybees); and 3) acute toxicity to aquatic organisms resulting from the use of EPN as a mosquito larvicide.

The Agency has quantitatively analyzed the risks of delayed neurotoxicity to humans from EPN residues on food and from applicator exposure. Based on a range of NOEL's and on an exposure study of EPN application to cotton, performed by Velsicol Chemical Corp., the Agency has determined that an ample margin of safety exists for the general population (dietary exposure), and for the following applicator groups: airplane pilots, mixer/loaders, and ground applicators. An ample margin of safety does not exist for flaggers, however.

Benefits resulting from the use of EPN were summarized in Table V-20. The largest benefits of use are on soybeans where benefits are estimated to range from $400,000 - $1,400,000 annually (1980 dollars) dependent on the level of use. Overall, individual growers on some sites would experience an increase in insecticidal treatment costs; however, aggregate user impacts range from negligible to minor, depending on the particular site, except in some localized regions where costs to users could be substantial. If EPN were cancelled economic impacts would not be expected at the processor and consumer level.

Based on its assessment of these risks and benefits, the Agency has determined that the registration of products for mosquito larvicide use can be cancelled without placing an unreasonable burden on the pest control community, and that application of products registered for the remaining uses can be continued, under certain conditions without subjecting man and the environment to unreasonable risk.

1. Risk/Benefit Analysis of Options

a. Cotton

The risks to human health and the environment which the Agency identified from EPN use on cotton are delayed neurotoxicity and reduction in populations of nontarget organisms (honeybees).

The Agency, based on its risk and benefit analyses, has concluded that the risks from of EPN use on cotton can be mitigated by implementing certain amendments to the terms and conditions of registration short of cancellation. This conclusion is based on the low exposure potential from use on cotton to the general population (dietary exposure) and to applicators (except flaggers). Although laboratory studies have demonstrated EPN's ability to induce delayed neurotoxic effects, levels of exposure to the general population and applicators (except flaggers) provide an ample margin of safety.

The Agency has determined that, since the risk to flaggers can be eliminated by regulatory action short of cancellation of the cotton use; since there is little or no risk to other exposed groups, this use should be retained even though the current benefits are negligible.

Human flaggers are sometimes used during aerial application of pesticides to serve as line-of-sight markers for the airplane pilot to apply the pesticide. In some instances, the flaggers are employed by the company applying the pesticide; more often, the farmer who owns the land serves as flagger for the applicator. Flaggers mark the approach path for the pilot either by standing in the field to be sprayed, or by driving a vehicle from point to point in, or around, the field. The Agency points out that, based on the Velsicol exposure study of EPN application to cotton (Velsicol, 1979b), there is not an ample margin of safety for human flaggers even when use of protective clothing and a respirator is assumed. Moreover, the Agency remains concerned about the possiblity of miscompliance with protective clothing requirements, since any flagger working without protective clothing and without the protection of an enclosed vehicle would be subject to dangerously high dermal and respiratory exposure. Flaggers who use trucks or other enclosed vehicles, however, to mark the approach path should be sufficiently protected from exposure in the enclosed vehicle to provide an ample margin of safety.

In addition, the Agency has determined that most flagging during aerial application of EPN to cotton is done by automatic, mechanical devices. Use of human flaggers appears not to represent standard practice and based on a recent survey conducted by the National Agricultural Aviation

Association (NAAA), most human flaggers reportedly mark approach paths by using enclosed vehicles (EPA, 1981n). Since the number of human flaggers who mark approach paths by standing in the field would appear to be small, and since alternative methods of flagging (either mechanical devices or flaggers in enclosed vehicles) exist and are already in use for EPN, prohibiting the use of human flaggers who are not protected by enclosed vehicles is not expected to have a significant economic impact on cotton growers who currently use EPN. Therefore, the Agency has determined to prohibit use of human flaggers during aerial application of EPN to cotton unless they are protected by totally enclosed vehicles (e.g., truck cab with all windows closed). In addition, as an added safety precaution, the Agency will require all applicators (except pilots and flaggers using enclosed vehicles) to wear specified protective clothing, goggles, and a respirator. The requirement for protective clothing will be required to be printed on the label, the phrase protective clothing required to appear in bold face type. Since most end-use formulations of EPN have been classified for restricted use, application of EPN will be restricted to certified applicators or those under their direct supervision. The Agency expects that certified applicators would already have and use, or have ready access to, the protective clothing required and the enclosed vehicle for flagging.

In addition, in order to prevent exposure to unprotected bystanders and nontarget organisms, the following statement must be printed in the "Use Directions" section of the label: "Do not apply this product when weather conditions favor drift from treated area."

With regard to the risk of reductions in populations of honeybees, the Agency has determined that there is an acute risk from EPN use on cotton; that sufficient residues persist for two to three days to present an acute risk; and that cotton blooms continually throughout the growing/application season.

Although no dollar value can be placed on commercial bee colonies or honey production in those areas where EPN is used on cotton, the Agency has concluded that the greatest potential for EPN damage to bees is in Tennessee and parts of Texas, where the number of commercial bee colonies is relatively large, and where EPN is an important insecticide for cotton (EPA, 1981m). Since cotton blooms throughout the growing season, it is not possible to reduce the risk to honeybees by limiting EPN application to times when cotton is not in bloom.

The Agency cannot, however, justify cancellation in this instance because of the localized nature of the potential problem (Texas and Tennessee); and the fact that the economic damage to commercial beekeepers from EPN use on cotton cannot be quantified. However, the Agency has determined that this hazard can be mitigated by implementing certain amendments to the terms and conditions of registration short of cancellation, and that this use should be retained.

b. Soybeans

The risks to human health and the environment which the Agency identified from EPN use on soybeans are delayed neurotoxicity and reduction in populations of nontarget organisms (honeybees).

The Agency, based on its risk and benefit analyses, has concluded that the benefits of EPN use on soybeans outweigh the risks, provided that certain amendments to the terms and conditions of registration are implemented, and that therefore this use should be retained. This conclusion is based on the following factors: the low exposure potential from use on soybeans to the general population (dietary exposure) and to applicators (except flaggers), and the negative economic impact on current EPN users should its use on soybeans be cancelled.

Although laboratory studies have demonstrated EPN's ability to induce delayed neurotoxic effects, levels of exposure to the general population and applicators (except flaggers) provide an ample margin of safety.

Given the low risk from current levels of exposure to EPN use on soybeans, the Agency considers that the corresponding benefits of this use outweigh the risks. Estimates of EPN use on soybeans range from about 203,000 to 685,000 acre-treatments annually. The bulk of EPN use on soybean acreage is concentrated in the Southcentral region. In any case, EPN's market share in this region does not exceed 20% of annual acre-treatments.

The Agency's discussion of risk to flaggers under cotton (above) also applies to soybeans. For the same reasons, the Agency has determined to retain the use of EPN on soybeans but to prohibit use of human flaggers unless they are in totally enclosed vehicles. In addition, as an added safety precaution, the Agency will require all applicators (except pilots and flaggers using enclosed vehicles) to wear specified protective clothing, goggles, and a respirator. The requirement for protective clothing will be required to be printed on the label, the phrase protective clothing required to appear in bold face type.

In addition, in order to prevent exposure to unprotected bystanders and nontarget organisms, the following statement must be printed in the "Use Directions" section of the label: "Do not apply this product when weather conditions favor drift from treated area."

With regard to the risk of reductions in populations of honeybees, the Agency has determined that there is an acute risk from EPN use on soybeans; that sufficient residue levels persist for two to three days to present an acute risk; and that soybeans are not an important bee forage crop.

Since soybeans are not an important bee forage crop, there does not appear to be significant exposure potential from EPN use on soybeans. Therefore, the Agency has determined to retain EPN use on soybeans and to mitigate whatever small risk to honeybees exists by implementing certain amendments to the terms and conditions of registration short of cancellation.

c. Field Corn

The risks to human health and the environment which the Agency identified from EPN use on field corn are delayed neurotoxicity and reduction in populations of nontarget organisms (honeybees).

The Agency, based on its risk and benefit analyses, has concluded that the risks from EPN use on field corn can be mitigated by implementing certain amendments to the terms and conditions of registration short of cancellation. This conclusion is based on the very low exposure potential from use on field corn to the general population (dietary exposure) and the low exposure potential to applicators (except flaggers).

The Agency has determined that, since the risk to flaggers can be eliminated by regulatory action short of cancellation of the field corn use; since there is little or no risk to other exposed groups, this use should be retained even though the current benefits are negligible.

The Agency's discussion of risk to flaggers under cotton (above) also applies to use on field corn. For the same reasons, the Agency has determined to retain the use of EPN on field corn but to prohibit use of human flaggers unless they are in totally enclosed vehicles. In addition, as an added safety precaution, the Agency will require all applicators (except pilots and flaggers using enclosed vehicles) to wear specified protective clothing, goggles, and a respirator. The requirement for protective clothing will be required to be printed on the label, the phrase protective clothing required to appear in bold face type.

In addition, in order to prevent exposure to unprotected bystanders and nontarget organisms, the following statement must be printed in the "Use Directions" section of the label: "Do not apply this product when weather conditions favor drift from treated area".

With regard to the risk of reductions in populations of honeybees, the Agency has determined that there is an acute risk from EPN use on field corn; that sufficient residue levels persist form two to three days to present an acute risk; that bees are not necessary for corn pollination but that they sometimes forage heavily for pollen; and that some EPN labels recommend applications during the pollen-shed period.

The Agency has determined to retain EPN use on field corn but to mitigate possible risk to honeybees by implementing certain amendments to the terms and conditions of registration short of cancellation.

d. Sweet Corn

The risks to human health and the environment which the Agency identified from EPN use on sweet corn are delayed neurotoxicity and reduction in populations of nontarget organisms (honeybees).

The Agency, based on its risk and benefits analyses, has concluded that the benefits of EPN use on sweet corn outweigh the risks, provided that certain amendments to the terms and conditions of registration are implemented, and that therefore this use should be retained. This conclusion is based on the following factors: the low exposure potential from use on sweet corn to the general population (dietary exposure) and to applicators (except flaggers), and the negative economic impact on current EPN users should its use on sweet corn be cancelled.

Given the low risk from current levels of exposure to EPN use on sweet corn, the Agency considers that the corresponding benefits outweigh the risks. A limited number of field trials in New York indicated that EPN was equal to or superior to methomyl and Penncap M® (encapsulated methyl parathion) for control of European corn borer, but further data are needed for a rigorous assessment of the relative efficacy of EPN and alternatives. Therefore, the Agency has assumed that the major alternatives are equally as effective as EPN for control of European corn borer on sweet corn.

In the Northcentral Region, EPN is primarily used in the granular formulation. In the Northeast, it is primarily used as an emulsifiable concentrate. In terms of cost per acre-treatment ($/acre-treatment), the 4% EPN granular costs $4.99; the 4 lb./gallon EC costs $2.23. The EPN EC formulation is less expensive on a unit basis than any alternative. In the Northcentral Region, cancellation of EPN would result in changed costs to growers ranging from a decrease of $2.63 per acre-treatment to an increase of $0.93 per acre-treatment. In the Northeast, cancellation of EPN would result in cost increases ranging from $0.40 to $3.69 per acre-treatment.

The Agency's discussion of risk to flaggers under cotton (above) also applies to use on sweet corn. For the same reasons, the Agency has determined to retain the use of EPN on sweet corn but to prohibit use of human flaggers unless they are in totally enclosed vehicles. In addition, as an added safety precaution, the Agency will require all applicators (except pilots and flaggers using enclosed vehicles) to wear specified protective clothing, goggles, and a respirator. The requirement for protective clothing will be required to be printed on the label, the phrase protective clothing required to appear in bold face type.

In addition, in order to prevent exposure to unprotected bystanders and nontarget organisms, the following statement must be printed in the "Use Directions" section of the label: "Do not apply this product when weather conditions favor drift from treated area".

With regard to risk of reduction in populations of honeybees, the Agency has determined that there is an acute risk from EPN use on sweet corn; that sufficient residues persist for two to three days to present an acute risk; that bees are not necessary for corn pollination but that they sometimes forage heavily for the pollen; that some labels recommend application during the pollen-shed period; and that for EPN use on sweet corn the greatest potential damage to bees is in New York state.

The Agency had determined that the benefits of EPN use on sweet corn outweigh the possible risks to honeybees, but that the risk can be mitigated without adverse economic impacts on EPN by implementing certain amendments to the terms and conditions of registration short of cancellation.

e. Pecans (Minor Use)

The risks to human health and the environment which the Agency has identified from EPN use on pecans are delayed neurotoxicity and reduction in populations of nontarget organisms (honeybees).

The Agency, based on its risks and benefit analyses, has concluded that the benefits of EPN use on pecans outweigh the risks, provided that certain amendments to the terms and conditions of registration are implemented, and that therefore this use should be retained. This conclusion is based on the following factors: the lack of exposure potential from use on pecans to the general population (dietary exposure), the low exposure potential to applicators (flaggers are not used), and the negative economic impact on current EPN users should its use on pecans be cancelled.

Given the low risk from current levels of exposure to EPN use on pecans, the Agency considers that the corresponding benefits outweigh the risks. The Agency estimates that EPN accounts for only about 3.4% of total acre-treatments made annually for pecan insects. Estimates of economic impacts, however, range from $164,000 to $173,000.

There are alternatives available which are as effective as EPN for control of the major pecan pests. Depending on the alternative recommended by various states, some alternatives are more expensive, others less expensive than EPN. For example, in Alabama all the alternatives to EPN (phosalone, dialifor, and carbaryl) are more expensive than EPN. In South Carolina, however, carbaryl, azinphos-methyl, dimethoate, and disulfoton are less expensive than EPN while phosalone and dialifor are more expensive.

The Agency will require all applicators (except pilots) to wear specified protective clothing, goggles, and a respirator. The requirement for protective clothing will be required to be printed on the label, the phrase protective clothing required to appear in bold face type.

In addition, in order to prevent exposure to unprotected bystanders and nontarget organisms, the following statement must be printed in the "Use Directions" section of the label: "Do not apply this product when weather conditions favor drift from treated area".

With regard to the risk of reduction in populations of honeybees, the Agency has determined that there is an acute risk from EPN use on pecans; that sufficient residues persist for two to three days to present an acute risk; that the greatest potential for EPN damage to bees from use on pecans is in Texas; and that EPN is not usually applied to blooming trees.

The Agency has determined that the benefits of EPN use on pecans outweigh the possible risks to honeybees, but that the risk can be mitigated without adverse economic impacts on EPN users by implementing certain amendments to the terms and conditions of registration short of cancellation.

f. Other Minor Food Uses

For all other registered food uses of EPN (except peaches), actual use of EPN is reported to be negligible. EPN is registered for use on the following food crops, in addition to those discussed above: almonds, apples, apricots, beans, beets, blackberries, boysenberries, cherries, citrus fruits, dewberries, grapes, lettuce, loganberries, nectarines, olives, peaches, pears, pineapples, plums (fresh prunes), quinces, raspberries, rutabagas, spinach, strawberries, sugar beets, tomatoes, turnips, walnuts, and youngberries. The Agency's best estimate is that current exposure and risk associated with the minor food uses of EPN are negligible since current usage is negligible. However, the Agency remains concerned about the potential risks, especially dietary risk to the general public, which could result if use patterns should significantly change such that significant amounts of EPN were used on all crops for which the pesticide is registered. While the Agency's best determination at this juncture is that current EPN usage on minor food crops is negligible, a degree of uncertainty about current use patterns has been raised by FDA findings of low-level residues (traces or parts per billion) in peanuts, baby food, apples, muffin mix, and trout.

Any discussion of potential risks and benefits, should EPN use on these crops increase in the future, must necessarily be general and speculative in nature. The Agency believes, however, that the following assumptions can be made about the potential risk and benefits of EPN if its use on any of the above listed crops should increase.

1) The general risks would be the same as discussed above for cotton, soybeans, field and sweet corn, and pecans (i.e., delayed neurotoxicity risk for humans, and risk of reductions in populations of nontarget organisms [honeybees]).

2) The levels of exposure for applicators would fall within the same range as discussed above for cotton (i.e., there would be an ample margin of safety for pilots, mixer/loaders, and ground applicators, but not for flaggers.)

3) Estimates of dietary exposure are more difficult, since such estimates would depend on the assumptions made about how many, and which, crops would experience increased EPN usage. However, as discussed in the dietary exposure analysis in Section IV of this document, if EPN were used

on all crops for which it is registered, and if residues occurred at tolerance levels, the resulting dietary exposure would most likely not present an ample margin of safety. However, The Agency considers this worst case scenario unlikely, since data on EPN residue levels for other crops, submitted in rebuttals, indicate that tolerance level exposure is unlikely. In addition, there are required preharvest intervals for several crops, so that residue levels would be further reduced.

4) Estimates of possible future benefits from EPN use are even more difficult, and certainly no dollar figure can be given. Nevertheless, some generalizations can be made. One of EPN's main advantages as an insecticide is its broad spectrum effectiveness (conversely, this is also a drawback since it kills beneficial insects as well). Since other pesticides currently used on these crops seem to be effective in pest control (otherwise one assumes EPN would be used in their stead), the argument in favor of retaining EPN registrations for these uses rests on the assumption that EPN would provide a useful tool in pest management programs should pest infestation levels increase or resistance to currently-used pesticides develop. If these uses for EPN were cancelled, a Section 18 emergency exemption could not be granted without first holding a hearing.

With the exception of worst-case dietary risk, in the event that EPN were present at tolerance levels on all crops for which it is registered, the levels of risk associated with possible future use of EPN are generally acceptable. The Agency has determined to retain registration for these uses provided that certain amendments to the terms and conditions of registration are imposed.

g. Mosquito Larvicide Use

The risk to the environment which the Agency has identified from EPN use as a mosquito larvicide is acute toxicity to aquatic organisms - i.e., when used according to label directions at recommended dosage rates, EPN products used as a mosquito larvicide exceed half the LC-50 for representative aquatic organisms likely to be exposed.

The Agency has also evaluated the economic benefits of EPN use as a mosquito larvicide and has determined that there would be negligible economic impacts if EPN were cancelled, because usage is negligible and is likely to remain so. There are several economic alternative pesticides available for this use.

The Agency, based on its risk and benefit analyses, has concluded that the risks of EPN use as a mosquito larvicide outweigh the benefits and that therefore this use should be cancelled. This conclusion is based on the following factors: the inherent acute risk to aquatic organisms from this use when EPN is used as directed on the label; the negligible economic impact of cancellation; the availability of several less toxic and economic alternatives; and the inability of other less rigorous regulatory options to reduce the risk to an acceptable level.

h. Additional Recommendations: All Food Uses

The Agency has determined that cancellation of minor food uses of EPN is not justifiable at this juncture. The Agency reaffirms its concern about potential dietary exposure and risk in connection with the possibility of a future scenario in which EPN is used on all crops for which it is registered and for which current tolerances are listed in 40 CFR 180.119. The data base to support EPN tolerances is not as complete as is required under present standard. Therefore, pursuant to the Pesticide Residue amendment to the Federal Food, Drug, and Cosmetic Act (Section 408), the administration of which is charged to the Environmental Protection Agency, the Agency will require data necessary to reassess EPN tolerances.

The Agency points our that worst-case dietary exposure based on tolerances for all crops could in all likelihood be reduced if EPN tolerances were reassessed and (wherever possible) lowered. Likewise EPN metabolites need to be taken into account.

E. Regulatory Decisions

This section sets forth the specific regulatory actions the Agency intends to take for the various uses of EPN.

1. Mosquito Larvicide Use

- Cancel, effective as of the statutorily prescribed 30-day period.

2. Cotton

- For aerial applications, flagging must be by fully automated mechanical means or by humans working in totally enclosed vehicles.

- Label requirements for protective clothing, goggles, and respirators must be standardized, the phrase protective clothing required to appear prominently in bold face type, as follows:

> PROTECTIVE CLOTHING REQUIRED: Wear clean protective clothing, goggles, and respirator approved by NIOSH or the American National Standards Institute when applying or handling, or when reentering fields within [at least 24] hours of treatment. The following protective clothing must be worn: lightweight, unlined,

natural rubber gloves at least mid-forearm in length; a wide brimmed waterproof hat or waterproof hood; a protective suit or coveralls of a non-permeable, non-cloth material covering the body from ankles to wrists; lightweight, unlined, natural rubber boots at least mid-calf in length; full-face respirators are recommended; half-face respirators and goggles are required.

Aerial applicators in positive pressure cockpits and other applicators in comparable ground equipment with appropriate filters at all air intakes need not comply with these protective clothing requirements.

- The following statements must appear in the "Use Directions" section of the label:

1) "Do not apply this product when weather conditions favor drift from treated area."

2) [applies to WP and EC formulations only] "Do not apply to blooming cotton if bees are visiting the treatment area."31/

31/ The Agency notes that the common practice of limiting application to early morning or late afternoon allows adherence to this labeling requirement as bees are not actively foraging at these times.

- The following statement must appear in the "Environmental Hazards" section of the label for WP and EC formulations: "This product is highly toxic to bees exposed to direct treatment or residues on blooming crops and weeds. Do not apply this product or allow it to drift to blooming crops or weeds if bees are visiting the treatment area."

3. Soybeans

- For aerial applications, flagging must be by fully automated mechanical means or by humans working in totally enclosed vehicles.

- Label requirements for protective clothing, goggles, and respirators must be standardized, the phrase protective clothing required to appear prominently in bold face type on the label. [Label statement given in full in Section VI.E.1. above.]

- The following statement must appear in the "Use Directions" section of the label:

"Do not apply this product when weather conditions favor drift from treated area."

- The following statement must appear in the "Environmental Hazards" section of the label for WP and EC formulations: "This product is highly toxic to bees exposed to direct treatment or residues on blooming crops and weeds. Do not apply this product or allow it to drift to blooming crops or weeds if bees are visiting the treatment area."

4. Field Corn

- For aerial applications, flagging must be by fully automated mechanical means or by humans working in totally enclosed vehicles.

- Label requirements for protective clothing, goggles, and respirators must be standardized, the phrase protective clothing required to appear prominently in bold face type. [Label statement given in full in Section VI.E.1. above.]

- The following statements must appear in the "Use Directions" section of the label:

1) "Do not apply this product when weather conditions favor drift from treated area."

2) [applies only to WP and EC formulations] "Do not apply to corn during the pollen-shed period if bees are visiting the treatment area."

- The following statement must appear in the "Environmental Hazards" section of the label for WP and EC formulations: "This product is highly toxic to bees exposed to direct treatment or residues on blooming crops and weeds. Do not apply this product or allow it to drift to blooming crops or weeds if bees are visiting the treatment area."

5. Sweet Corn

- For aerial applications, flagging must be by fully automated mechanical means or by humans working in totally enclosed vehicles.

- Label requirements for protective clothing, goggles, and respirators must be standardized, the phrase protective clothing required to appear prominently in bold face type on the label. [Label statement given in full in Section VI.E.1. above.]

- The following statements must appear in the "Use Directions" section of the label:

1) "Do not apply this product when weather conditions favor drift from treated area."

2) [applies only to WP and EC formulations] "Do not apply to corn during the pollen-shed period if bees are visiting the treatment area."

- The following statement must appear in the "Environmental Hazards" section of the label for WP and EC formulations: "This product is highly toxic to bees exposed to direct treatment or residues on blooming crops and weeds. Do not apply this product or allow it to drift to blooming crops or weeds if bees are visiting the treatment area."

5. Pecans

- Label requirements for protective clothing, goggles, and respirators must be standardized, the phrase protective clothing required to appear prominently in bold face type. [Label statement given in full in Section VI.E.1. above.]

- The following statement must appear in the "Use Directions" section of the label:

"Do not apply this product when weather conditions favor drift from treated area."

- The following statement must appear in the "Environmental Hazards" section of the label for WP and EC formulations: "This product is highly toxic to bees exposed to direct treatment or residues on blooming crops and weeds. Do not apply this product or allow it to drift to blooming crops or weeds if bees are visiting the treatment area."

7. Other Food Uses

- For aerial applications, flagging must be by fully automated mechanical means or by humans working in totally enclosed vehicles.

- Label requirements for protective clothing, goggles, and respirators must be standardized, the phrase protective clothing required to appear prominently in bold face type on the label. [Label statement given in full in Section VI.E.1. above.]

- The following statements must appear in the "Use Directions" section of the label:

1) "Do not apply this product when weather conditions favor drift from treated area."

2) [applies only to WP and EC formulations labeled for use on stone fruits, pome fruits, and citrus] "Do not apply when trees or a substantial number of weeds in the orchard/grove are in bloom."

- The following statement must appear in the "Environmental Hazards" section of the label for WP and EC formulations: "This product is highly toxic to bees exposed to direct treatment or residues on blooming crops and weeds. Do not apply this product or allow it to drift to blooming crops or weeds if bees are visiting the treatment area."

8. Other Recommendations -- All Food Uses

- Pursuant to Section 408 of the Federal Food, Drug, and Cosmetic Act, the Administrator may establish tolerances for residues of a pesticide on raw agricultural commodities. Compliance with these tolerances is monitored by the Food and Drug Administration and the Department of Agriculture. The Agency has determined that EPN tolerances require reassessment. Data necessary to reassess EPN tolerances will be required.

9. Areas for Further Consideration

The Agency has identified areas of concern for which no data exists or for which additional data are needed. The Agency will require these gaps to be filled. The areas of concern and the data needed are:

Teratogenic Effects

Teratogenic studies in rats and rabbits.

Oncogenic Effects

Studies on the oncogenic potential of EPN.

Delayed Neurotoxic Effects

The Agency will require a study to explore the mechanism of "recovery" from a mild case of EPN induced delayed neurotoxicity in an experimental animal species. The study should be designed to distinguish between regrowth and/or repair of damaged axons or compensation by learning to use the remaining functional system. Use of a combination of electrophysiological and histopathological methodology will be considered. The possibility of using a species other than the chicken will also be considered based on the recent Abou-Donia et al. (1983) demonstration of EPN delayed neurotoxicity in the cat.

Re-entry Time Reassessment

The Agency has determined that the 24 hour re-entry time established for EPN requires reassessment. Data necessary to reassess the re-entry time for EPN will be required.

Table VI-1 below summarizes the Agency's final regulatory decision on EPN.

Table VI-1. Summary of Final Regulatory Decision on EPN

Use Site	Final Decision
Mosquito Larvicide Use	- Cancel, effective as of the end of the statutorily prescribed 30-day period.
All Other Uses	- Cancel, unless the following modifications are made to the terms and conditions of registration. - Human flaggers prohibited unless in totally enclosed vehicles. - Standardize label requirements for protective clothing, goggles, and respirators, the phrase protective clothing required to appear prominently in bold face type, as follows: PROTECTIVE CLOTHING REQUIRED: Wear clean protective clothing, goggles, and respirator approved by NIOSH or the American National Standards Institute when applying or handling, or when reentering fields within [at least 24] hours of treatment. The following protective clothing must be worn: lightweight unlined natural rubber gloves at least mid-forearm in length; a wide brimmed waterproof hat or waterproof hood; a protective suit or coveralls of a non-permeable, non-cloth material covering the body from ankles to wrists; lightweight unlined natural rubber boots at least mid-calf in length; full-face respirators are recommended; half-face respirators and goggles are required. - The following statement must appear in the "Use Directions" section of the label: "Do not apply this product when weather conditions favor drift from treated area."

Table VI-1 Continued. Summary of Final Regulatory Decision on EPN

Use Site	Final Decision
	- The following statement must appear in the "Environmental Hazards" section of the label for WP and EC formulations: "This product is highly toxic to bees exposed to direct treatment or residues on blooming crops or weeds. Do not apply this product or allow it to drift to blooming crops or weeds if bees are visiting the treatment area."
WP and EC formulations for use on Cotton	- In addition to the requirements for "All Uses", the following statement must appear in the "Use Directions" section of the label: "Do not apply to blooming cotton if bees are visiting the treatment area."
WP and EC formulations for use on Field Corn and/or sweet corn	- In addition to the requirements for "All Uses," the following statement must appear in the "Use Directions" section of the label: "Do not apply to corn during the pollen-shed period if bees are visiting the treatment areas."
WP and EC Formulations for use on stone fruits, pome fruits, and citrus	- In addition to the requirements for "All Uses," the following statement must appear in the "Use Directions" section of the label: - "Do not apply when trees or a substantial number of weeds in the orchard/grove are in bloom."
All Food Uses	- Reassess tolerances. Data necessary to reassess EPN tolerances will be required in the Agency's Registration Standards Review Process.
Areas for Further Consideration	- Teratogenic effects - Oncogenic effect - Delayed neurotoxic effect - Re-entry

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*/ Copies of references not designated confidential will be provided on request. There will be a charge to cover duplicating costs for each request. A copy of the Position Document and all references not designated confidential are available for public inspection in the Special Pesticide Review Division (TS-791), Office of Pesticide Programs, Environmental Protection Agency, Crystal Mall #2, Room 722, 1921 Jefferson Davis Highway, Crystal City, Virginia 22202.

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